

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
17 May 2001 (17.05.2001)

PCT

(10) International Publication Number  
WO 01/34802 A2

(51) International Patent Classification<sup>7</sup>: C12N 15/12,  
15/62, 15/11, 1/21, 5/10, C07K 14/47, 16/18, 19/00, A61K  
38/17, 31/70, 39/395, 48/00, G01N 33/68, C12Q 1/68

(21) International Application Number: PCT/US00/30904

(22) International Filing Date:  
9 November 2000 (09.11.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
09/439,313 12 November 1999 (12.11.1999) US  
09/443,686 18 November 1999 (18.11.1999) US

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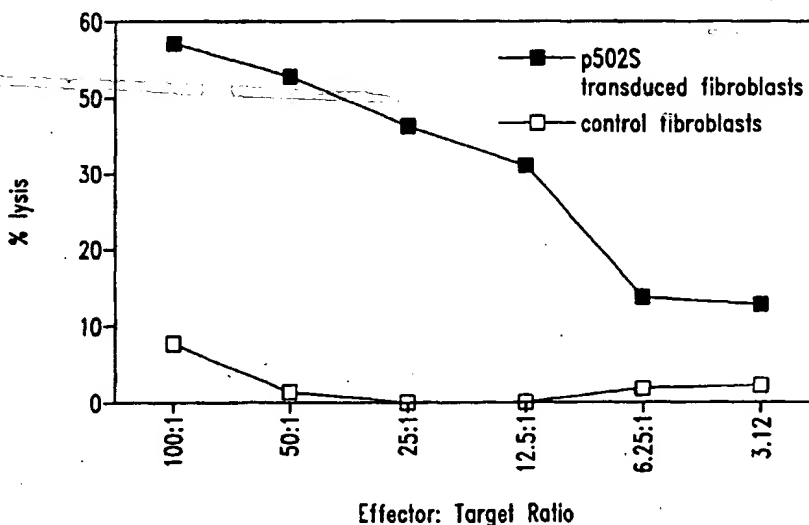
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(81) Designated States (national): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,

[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.

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DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) **Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,

IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— *Without international search report and to be republished upon receipt of that report.*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

## COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

### 5 TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for  
10 prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

### BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress  
15 inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but  
20 these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate  
25 with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

### 30 SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the

diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate-specific protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-550.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate-specific protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate-specific protein; and (b) a physiologically acceptable carrier. In certain embodiments, the present invention provides monoclonal antibodies that specifically bind to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 522 and 541-550, together with monoclonal antibodies comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.



Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

5           Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

10           Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

15           Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that  
20 specifically react with a prostate-specific protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described  
25 above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time  
30 sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate-specific protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

10 Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

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The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

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The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain

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embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that  
5 hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b)  
10 detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as  
15 monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed  
20 herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

#### BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The  
25 percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure  
30 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

5 Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

10 Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

15 Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

20 Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

25 Figure 11 shows the results of an ELISA assay of antibody specificity to P501S peptides.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12

SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16

30 SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1

SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9

SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4

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SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280

SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S)

5

SEQ ID NO: 108 is the predicted amino acid sequence for F1-12

SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17

SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as

10 P503S)

SEQ ID NO: 112 is the predicted amino acid sequence for J1-17

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25 SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811  
SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-4876  
SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-4884  
SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-4896  
SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-4761  
30 SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-4762  
SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-4766  
SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770

- SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771
- SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-4772
- SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-4309
- SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278
- 5 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288
- SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283
- SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304
- SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296
- SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280
- 10 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
- SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
- SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
- SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
- SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
- 15 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd
- SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev
- SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd
- SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev
- SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd
- 20 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev
- SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd
- SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev
- SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev
- SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd
- 25 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev
- SEQ ID NO: 223 is the determined cDNA sequence for P509S
- SEQ ID NO: 224 is the determined cDNA sequence for P510S
- SEQ ID NO: 225 is the determined cDNA sequence for P703DE5
- SEQ ID NO: 226 is the determined cDNA sequence for 9-A11
- 30 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6
- SEQ ID NO: 228 is the determined cDNA sequence for 8-H7
- SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13

- SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14  
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23  
SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24  
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25  
5 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30  
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34  
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35  
SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36  
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38  
10 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39  
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40  
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41  
SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42  
SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45  
15 SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46  
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51  
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56  
SEQ ID NO: 247 is the determined cDNA sequence for PTPN64  
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65  
20 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67  
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76  
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84  
SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85  
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86  
25 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87  
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88  
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1  
SEQ ID NO: 257 is the determined cDNA sequence for JP1F2  
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2  
30 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1  
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2  
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3

- SEQ ID NO: 262 is the determined cDNA sequence for JP1A4  
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5  
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6  
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6  
5 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5  
SEQ ID NO: 267 is the determined cDNA sequence for JP1A6  
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8  
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7  
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9  
10 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10  
SEQ ID NO: 272 is the determined cDNA sequence for JP1A9  
SEQ ID NO: 273 is the determined cDNA sequence for JP1F12  
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12  
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11  
15 SEQ ID NO: 276 is the determined cDNA sequence for JP1C11  
SEQ ID NO: 277 is the determined cDNA sequence for JP1C12  
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12  
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12  
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2  
20 SEQ ID NO: 281 is the determined cDNA sequence for JP8H1  
SEQ ID NO: 282 is the determined cDNA sequence for JP8H2  
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3  
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4  
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3  
25 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4  
SEQ ID NO: 287 is the determined cDNA sequence for JP8B6  
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6  
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5  
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8  
30 SEQ ID NO: 291 is the determined cDNA sequence for JP8C7  
SEQ ID NO: 292 is the determined cDNA sequence for JP8D7  
SEQ ID NO: 293 is the determined cDNA sequence for P8D8

- SEQ ID NO: 294 is the determined cDNA sequence for JP8E7  
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8  
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8  
SEQ ID NO: 297 is the determined cDNA sequence for JP8B10  
5 SEQ ID NO: 298 is the determined cDNA sequence for JP8C10  
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9  
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10  
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9  
SEQ ID NO: 302 is the determined cDNA sequence for JP8H9  
10 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12  
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11  
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12  
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12  
SEQ ID NO: 307 is the determined cDNA sequence for P711P  
15 SEQ ID NO: 308 is the determined cDNA sequence for P712P  
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23  
SEQ ID NO: 310 is the determined cDNA sequence for P774P  
SEQ ID NO: 311 is the determined cDNA sequence for P775P  
SEQ ID NO: 312 is the determined cDNA sequence for P715P  
20 SEQ ID NO: 313 is the determined cDNA sequence for P710P  
SEQ ID NO: 314 is the determined cDNA sequence for P767P  
SEQ ID NO: 315 is the determined cDNA sequence for P768P  
SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes  
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5  
25 SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5  
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26  
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26  
SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23  
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23  
30 SEQ ID NO: 332 is the determined full length cDNA sequence for P509S  
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)  
SEQ ID NO: 334 is the determined cDNA sequence for P714P

- SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)
- SEQ ID NO: 336 is the predicted amino acid sequence for P705P
- SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10
- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- 5 SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo
- 10 sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin
- 15 SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)
- SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)
- SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo
- 20 sapiens phosphoglucomutase-related protein (PGMRP)
- SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40
- SEQ ID NO: 350 is the determined cDNA sequence for P777P
- SEQ ID NO: 351 is the determined cDNA sequence for P779P
- 25 SEQ ID NO: 352 is the determined cDNA sequence for P790P
- SEQ ID NO: 353 is the determined cDNA sequence for P784P
- SEQ ID NO: 354 is the determined cDNA sequence for P776P
- SEQ ID NO: 355 is the determined cDNA sequence for P780P
- SEQ ID NO: 356 is the determined cDNA sequence for P544S
- 30 SEQ ID NO: 357 is the determined cDNA sequence for P745S
- SEQ ID NO: 358 is the determined cDNA sequence for P782P
- SEQ ID NO: 359 is the determined cDNA sequence for P783P

- SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984
- SEQ ID NO: 361 is the determined cDNA sequence for P787P
- SEQ ID NO: 362 is the determined cDNA sequence for P788P
- SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994
- 5 SEQ ID NO: 364 is the determined cDNA sequence for P781P
- SEQ ID NO: 365 is the determined cDNA sequence for P785P
- SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.
- SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.
- 10 SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.
- SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.
- SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.
- 15 SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.
- SEQ ID NO: 381 is the determined cDNA sequence for B716P.
- SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.
- 20 SEQ ID NO: 383 is the predicted amino acid sequence for P711P.
- SEQ ID NO: 384 is the cDNA sequence for P1000C.
- SEQ ID NO: 385 is the cDNA sequence for CGI-82.
- SEQ ID NO: 386 is the cDNA sequence for 23320.
- SEQ ID NO: 387 is the cDNA sequence for CGI-69.
- 25 SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.
- SEQ ID NO: 389 is the cDNA sequence for 23379.
- SEQ ID NO: 390 is the cDNA sequence for 23381.
- SEQ ID NO: 391 is the cDNA sequence for KIAA0122.
- SEQ ID NO: 392 is the cDNA sequence for 23399.
- 30 SEQ ID NO: 393 is the cDNA sequence for a previously identified gene.
- SEQ ID NO: 394 is the cDNA sequence for HCLBP.
- SEQ ID NO: 395 is the cDNA sequence for transglutaminase.



- SEQ ID NO:396 is the cDNA sequence for a previously identified gene.
- SEQ ID NO:397 is the cDNA sequence for PAP.
- SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.
- SEQ ID NO:399 is the cDNA sequence for hTGR.
- 5 SEQ ID NO:400 is the cDNA sequence for KIAA0295.
- SEQ ID NO:401 is the cDNA sequence for 22545.
- SEQ ID NO:402 is the cDNA sequence for 22547.
- SEQ ID NO:403 is the cDNA sequence for 22548.
- SEQ ID NO:404 is the cDNA sequence for 22550.
- 10 SEQ ID NO:405 is the cDNA sequence for 22551.
- SEQ ID NO:406 is the cDNA sequence for 22552.
- SEQ ID NO:407 is the cDNA sequence for 22553.
- SEQ ID NO:408 is the cDNA sequence for 22558.
- SEQ ID NO:409 is the cDNA sequence for 22562.
- 15 SEQ ID NO:410 is the cDNA sequence for 22565.
- SEQ ID NO:411 is the cDNA sequence for 22567.
- SEQ ID NO:412 is the cDNA sequence for 22568.
- SEQ ID NO:413 is the cDNA sequence for 22570.
- SEQ ID NO:414 is the cDNA sequence for 22571.
- 20 SEQ ID NO:415 is the cDNA sequence for 22572.
- SEQ ID NO:416 is the cDNA sequence for 22573.
- SEQ ID NO:417 is the cDNA sequence for 22573.
- SEQ ID NO:418 is the cDNA sequence for 22575.
- SEQ ID NO:419 is the cDNA sequence for 22580.
- 25 SEQ ID NO:420 is the cDNA sequence for 22581.
- SEQ ID NO:421 is the cDNA sequence for 22582.
- SEQ ID NO:422 is the cDNA sequence for 22583.
- SEQ ID NO:423 is the cDNA sequence for 22584.
- SEQ ID NO:424 is the cDNA sequence for 22585.
- 30 SEQ ID NO:425 is the cDNA sequence for 22586.
- SEQ ID NO:426 is the cDNA sequence for 22587.
- SEQ ID NO:427 is the cDNA sequence for 22588.

- SEQ ID NO:428 is the cDNA sequence for 22589.  
SEQ ID NO:429 is the cDNA sequence for 22590.  
SEQ ID NO:430 is the cDNA sequence for 22591.  
SEQ ID NO:431 is the cDNA sequence for 22592.  
5 SEQ ID NO:432 is the cDNA sequence for 22593.  
SEQ ID NO:433 is the cDNA sequence for 22594.  
SEQ ID NO:434 is the cDNA sequence for 22595.  
SEQ ID NO:435 is the cDNA sequence for 22596.  
SEQ ID NO:436 is the cDNA sequence for 22847.  
10 SEQ ID NO:437 is the cDNA sequence for 22848.  
SEQ ID NO:438 is the cDNA sequence for 22849.  
SEQ ID NO:439 is the cDNA sequence for 22851.  
SEQ ID NO:440 is the cDNA sequence for 22852.  
SEQ ID NO:441 is the cDNA sequence for 22853.  
15 SEQ ID NO:442 is the cDNA sequence for 22854.  
SEQ ID NO:443 is the cDNA sequence for 22855.  
SEQ ID NO:444 is the cDNA sequence for 22856.  
SEQ ID NO:445 is the cDNA sequence for 22857.  
SEQ ID NO:446 is the cDNA sequence for 23601.  
20 SEQ ID NO:447 is the cDNA sequence for 23602.  
SEQ ID NO:448 is the cDNA sequence for 23605.  
SEQ ID NO:449 is the cDNA sequence for 23606.  
SEQ ID NO:450 is the cDNA sequence for 23612.  
SEQ ID NO:451 is the cDNA sequence for 23614.  
25 SEQ ID NO:452 is the cDNA sequence for 23618.  
SEQ ID NO:453 is the cDNA sequence for 23622.  
SEQ ID NO:454 is the cDNA sequence for folate hydrolase.  
SEQ ID NO:455 is the cDNA sequence for LIM protein.  
SEQ ID NO:456 is the cDNA sequence for a known gene.  
30 SEQ ID NO:457 is the cDNA sequence for a known gene.  
SEQ ID NO:458 is the cDNA sequence for a previously identified gene.  
SEQ ID NO:459 is the cDNA sequence for 23045.

- SEQ ID NO:460 is the cDNA sequence for 23032.
- SEQ ID NO:461 is the cDNA sequence for 23054.
- SEQ ID NO:462-467 are cDNA sequences for known genes.
- SEQ ID NO:468-471 are cDNA sequences for P710P.
- 5 SEQ ID NO:472 is a cDNA sequence for P1001C.
- SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).
- SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).
- 10 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).
- SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).
- SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO:
- 15 474.
- SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.
- 20 SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.
- SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.
- SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO:
- 25 473.
- SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.
- SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.
- SEQ ID NO: 485 is the PCR primer AW025.
- 30 SEQ ID NO: 486 is the PCR primer AW003.
- SEQ ID NO: 487 is the PCR primer AW027.
- SEQ ID NO: 488 is the PCR primer AW026.

SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

5 SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.

SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

10 SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

15 SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P. SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.

SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.

SEQ ID NO: 526 is the full-length cDNA sequence for P790P.

SEQ ID NO: 527 is the predicted amino acid sequence for P790P.

SEQ ID NO: 528 & 529 are PCR primers.

20 SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.

SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.

SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.

SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.

SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.

25 SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.

SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.

SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.

SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.

SEQ ID NO: 539 is the peptide P501S-370.

30 SEQ ID NO: 540 is the peptide P501S-376.

SEQ ID NO: 541-550 are epitopes of P501S.

SEQ ID NO: 551 corresponds to amino acids 543-553 of P501S.

## DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate-specific polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate-specific protein or a variant thereof. A "prostate-specific protein" is a protein that is expressed in normal prostate and/or prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a non-prostate normal tissue, as determined using a representative assay provided herein. Certain prostate-specific proteins are proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate-specific proteins. Sequences of polynucleotides encoding certain prostate-specific proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Sequences of polypeptides comprising at least a portion of a prostate-specific protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

## PROSTATE-SPECIFIC PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate-specific protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred

polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate-specific protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate-specific protein. Polynucleotides complementary to any such sequences are also  
5 encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the  
10 present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate-specific protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions,  
15 and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate-specific protein or a portion thereof. The  
20 term "variants" also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local  
25 regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the  
30 Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices

for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) *Unified Approach to Alignment and Phylogenesis* pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Preferably, the “percentage of sequence identity” is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate-specific protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such

as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate-specific than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate-specific cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate-specific cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with  $^{32}\text{P}$ ) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into



a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments; using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate-specific protein are provided in SEQ ID NO:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536.

Isolation of these polynucleotides is described below. Each of these prostate-specific proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis.

5 Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate-specific protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain

10 portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (*e.g.*, by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate-specific polypeptide, and administering the transfected cells to the patient).

15 A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a protein. Antisense technology can be used to control gene expression

20 through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In* Huber and Carr, *Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (*e.g.*, promoter, enhancer or transcription initiation site), and block transcription of

25 the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30

30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3'

ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

5 Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector  
10 will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for  
15 therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). The polynucleotides may also be administered as naked plasmid vectors.  
20 Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary  
25 skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane  
30 vesicle). The preparation and use of such systems is well known in the art.

## PROSTATE-SPECIFIC POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate-specific protein or a variant thereof, as described herein. As noted above, a "prostate-specific protein" is a protein that is expressed by normal prostate and/or prostate tumor cells. Proteins that are prostate-specific proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate-specific protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate-specific protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the

immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate-specific protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate-specific protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino

acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Peptides and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known prostate-specific protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner),

preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are

located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

5 Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 10 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The 15 lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as 20 LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been 25 exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion 30 incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its



original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector  
5 that is not a part of the natural environment.

#### BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate-specific protein. As used herein, an  
10 antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate-specific protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate-specific protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding  
15 constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about  $10^3$  L/mol. The binding constant may be determined using methods well known in the art.

20 Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate-specific protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals  
25 without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the  
30 above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Most preferably, antibodies employed in the inventive methods have the ability to induce lysis of tumor cells by activation of complement and mediation of antibody-dependent cellular cytotoxicity (ADCC). Antibodies of different classes and subclasses differ in these properties. For example, mouse antibodies of the IgG2a and IgG3 classes are capable of activating serum complement upon binding to target cells which express the antigen against which the antibodies were raised, and can mediate ADCC.

Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells

and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are  
5 selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse.  
10 Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

The preparation of mouse and rabbit monoclonal antibodies that specifically bind to  
15 polypeptides of the present invention is described in detail below. However, the antibodies of the present invention are not limited to those derived from mice. Human antibodies may also be employed in the inventive methods and may prove to be preferable. Such antibodies can be obtained using human hybridomas as described by Cote *et al.* (Monoclonal Antibodies and Cancer Therapy, Alan R. Lisa, p. 77, 1985). The present invention also encompasses antibodies made by  
20 recombinant means such as chimeric antibodies, wherein the variable region and constant region are derived from different species, and CDR-grafted antibodies, wherein the complementarity determining region is derived from a different species, as described in US Patents 4,816,567 and 5,225,539. Chimeric antibodies may be prepared by splicing genes for a mouse antibody molecule having a desired antigen specificity together with genes for a human antibody molecule having the  
25 desired biological activity, such as activation of human complement and mediation of ADCC (Morrison *et al. Proc. Natl. Acad. Sci. USA* 81:6851, 1984; Neuberger *et al. Nature* 312:604, 1984; Takeda *et al. Nature* 314:452, 1985).

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard  
30 techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*,

Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to

Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

5           It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or  
10   linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

          A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent  
15   No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating  
20   compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

          A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of  
25   a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

#### T CELLS

30           Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate-specific protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral

blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from Nexell Therapeutics Inc., Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated  
5 humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate-specific polypeptide, polynucleotide encoding a prostate-specific polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate-specific  
10 polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate-specific polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a  
15 variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell  
20 proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate-specific polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of  
25 the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate-specific polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Prostate-specific protein-specific T cells may be expanded using  
30 standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a prostate-specific polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate-specific polypeptide, or a short peptide  
5 corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate-specific polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate-specific protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

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#### PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds  
15 and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally  
20 described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the  
25 composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression  
30 systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression

in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA



or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- $\gamma$ , TNF $\alpha$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10 ) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example,

an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent  
5 adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release  
10 formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix  
15 and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical  
20 compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the  
25 antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or  
30 progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy,

*Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take-up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface  
5 receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone  
10 marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into  
15 dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this  
20 nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc $\gamma$  receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II  
25 MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a prostate-specific protein (or portion or other variant thereof) such that the prostate-specific polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex*  
30 *vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection

that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells  
5 with the prostate-specific polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of  
10 the polypeptide.

#### CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical  
15 compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor.  
20 Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react  
25 against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not  
30 necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer

cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate  
5 antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in*  
10 *vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte,  
15 fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies  
20 have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back  
25 into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established  
30 using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered

over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50%  
5 above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-  
10 vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25  $\mu$ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active  
15 compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate-specific protein generally correlate with an improved clinical outcome. Such immune responses may generally be  
20 evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or  
25 more prostate-specific proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the  
30 agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer.

In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g., Harlow and Lane, 5 Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized  
10 on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G,  
15 protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full  
20 length prostate-specific proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or  
25 disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization"  
30 refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a

membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of  
5 binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the  
10 binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may  
15 be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The  
20 amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween  
25 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer.  
30 Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by



assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains  
5 a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of  
10 time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group,  
15 (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a  
20 signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is  
25 determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest  
30 to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along

the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1  $\mu$ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate-specific polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate-specific protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate-specific protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a prostate-specific polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that

expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may  
5 be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate-specific polypeptide (*e.g.*, 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate-specific polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater  
10 and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate-specific protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to  
15 amplify a portion of a prostate-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate-specific protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate-specific protein may be used in a hybridization  
20 assay to detect the presence of polynucleotide encoding the protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate-specific protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in  
25 length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15  
30 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Techniques for both PCR based assays and hybridization assays

are well known in the art (*see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989*).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate-specific protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for proteins provided herein may be combined with assays for other known tumor antigens.

## DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate-specific protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate-specific protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate-specific protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate-specific protein.

The following Examples are offered by way of illustration and not by way of limitation.

## EXAMPLES

### EXAMPLE 1

#### 5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate  
10 tumor poly A<sup>+</sup> RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA was then purified using a Qiagen oligotex spin column mRNA  
15 purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into  
20 ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained  $1.64 \times 10^7$   
25 independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained  $3.3 \times 10^6$  independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

30 cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as

follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H<sub>2</sub>O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As  
5 recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H<sub>2</sub>O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with  
10 BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H<sub>2</sub>O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and  
15 incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H<sub>2</sub>O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA  
20 was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and  
25 grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively,  
30 with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1  $\mu$ g each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA



library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show  
5 some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid  
10 sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided  
15 in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating  
20 sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in  
30 SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated

clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA<sup>+</sup> RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni,

Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively.

## EXAMPLE 2

### DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2 µg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using β-actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β-actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for each

reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney,

but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following  
5 normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues  
10 tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. ID-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in  
15 normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in  
20 prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and  
25 expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was  
30 found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

### EXAMPLE 3

#### ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of

2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.



An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX\_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. The putative full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 525.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483.

Subsequent studies led to the identification of a genomic region on chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led

to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

#### EXAMPLE 4

##### SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18-reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

#### EXAMPLE 5

##### FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the

subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most

recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350, 351 and 353-365.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

## EXAMPLE 6

## PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

5 6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID  
10 NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (RPMI-1640; Gibco  
15 BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL),  $2 \times 10^{-5}$  M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells ( $5 \times$   
20  $10^5$ /ml) were restimulated with  $2.5 \times 10^6$ /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb  
25 tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in  
30 Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice  
5 were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2  
10 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on  
15 the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2Kb were immunized as described  
20 by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A<sup>b</sup> binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (as described above) and cultured  
25 in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells ( $5 \times 10^5$ /ml) were restimulated with  $2.5 \times 10^6$ /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were  
30 restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

#### EXAMPLE 7

##### 10 PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100  $\mu$ g P501S in the vector VR1012 either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed HLA-A2-restricted CTL epitope.

#### EXAMPLE 8

##### 25 ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8<sup>+</sup> T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8<sup>+</sup> T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a  $\gamma$ -interferon



ELISPOT assay (*see* Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on  $10^4$  fibroblasts in the presence of 3  $\mu\text{g/ml}$  human  $\beta_2$ -microglobulin and 1  $\mu\text{g/ml}$  P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the fibroblasts were treated with 10 ng/ml  $\gamma$ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a  $\gamma$ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

20

## EXAMPLE 9

ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES  
IN HUMAN BLOOD

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GM-CSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8<sup>+</sup> cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts retrovirally transduced

to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays ( $^{51}\text{Cr}$  release) and interferon-gamma production (Interferon-gamma Elispot; *see* above and Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

#### EXAMPLE 10

##### IDENTIFICATION OF A NATURALLY PROCESSED CTL EPIOTOPE CONTAINED WITHIN A PROSTATE-SPECIFIC ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100  $\mu\text{g}$  of p5 peptide together with 140  $\mu\text{g}$  of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived

from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 ug/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

#### EXAMPLE 11

##### 10                   EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN                           IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in  
15   SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of  
SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is provided in  
20   SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly  
25   expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).

#### EXAMPLE 12

##### 30                   GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND                           STIMULATION TECHNIQUES WITH PROSTATE-SPECIFIC ANTIGEN

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- $\gamma$  ELISPOT analysis as described above. Using a panel of  
5 HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a  
10 multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3  $\mu$ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that  
15 specifically produced interferon- $\gamma$  when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- $\gamma$  in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

20 To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN- $\gamma$  ELISPOT assays against these A2Kb targets transduced with the "library" of P501S  
25 fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were  
30 also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN- $\gamma$  assay. Only peptides

P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

5 In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8+ T cells were cultured with autologous CD40  
10 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as  
15 demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-  
20 P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

### EXAMPLE 13

#### IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

25

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in  
30 prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences

SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

5

Table I  
Summary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-Iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97%

of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

#### EXAMPLE 14

##### IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which



expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II

Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups:

10 Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group

15 libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (*see* Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III  
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV  
Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
439	22851	PAP

440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

#### EXAMPLE 15

#### FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-461 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences.

#### EXAMPLE 16

#### FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane

filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four  
5 sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene.

## EXAMPLE 17

### PROTEIN EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

10

This example describes the expression and purification of the prostate-specific antigen P501S in *E. coli*, baculovirus and mammalian cells.

#### a) Expression in *E. coli*

15 Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an  
20 antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min,  
25 and lastly by 1 cycle of 72°C for 10 min. The PCR product was cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was  
30 induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A

(Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

5           An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR  
10 product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

          The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands,  
15 were also observed, probably due to aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

          A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen  
20 Ra12 (SEQ ID NO: 484) was prepared as follows. P501S DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

25           The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD\_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c) Expression of P501S in mammalian cells

Full-length P501S (553AA) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The Fugene/DNA mixture

was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15  $\mu$ l of GenePorter was diluted in 500  $\mu$ l of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2  $\mu$ g of plasmid DNA that was diluted in 500  $\mu$ l of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

#### EXAMPLE 18

##### PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

###### **a) Preparation and Characterization of Antibodies against P501S**

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to



generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

## Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant ( $\mu\text{g/ml}$ )
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1  $\mu\text{g/ml}$ , followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate

specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate-tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr.

HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab') fragment (Jackson ImmunoResearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

#### **b) Preparation and Characterization of Antibodies against P503S**

A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits

and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows.

The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further

15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception  
5 of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

10 Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat  
15 anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal,  
20 breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary,  
25 pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal  
30 antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the

appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

5 **c) Preparation and Characterization of Antibodies against P703P**

Rabbits were immunized with either a truncated (P703Ptrl; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptrl attached to a solid support. Rabbit monoclonal  
10 antibodies were isolated using SLAM technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal  
20 antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

25 The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk<sup>-/-</sup> cells either untransfected or transfected with a plasmid

expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

#### EXAMPLE 19

##### CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains. Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as

described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparagine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (i.e. intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM



sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above.

To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server (<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al. Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

## CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536;

(b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and

(c) complements of any of the sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID No: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

4. An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a prostate-specific protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the protein  
5 comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413,  
10 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate-specific protein, or a  
15 variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396,  
20 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide comprising a sequence recited in any one  
25 of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530,  
30 531, 533, 535 and 536.

7. An isolated polynucleotide comprising a sequence that hybridizes under moderately stringent conditions to a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector comprising a polynucleotide according to any one of claims 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate-specific protein, the protein comprising an amino acid sequence encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536 or a complement of any of the foregoing polynucleotide sequences.

12. A monoclonal antibody that specifically binds to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 519, 520, 522 and 539-551.

5 13. A monoclonal antibody comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

14. A fusion protein comprising at least one polypeptide according to  
10 claim 1.

15 15. A fusion protein according to claim 14, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

16 16. A fusion protein according to claim 14, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

17 17. A fusion protein according to claim 14, wherein the fusion protein  
20 comprises an affinity tag.

18. An isolated polynucleotide encoding a fusion protein according to claim 14.

25 19.. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

- (a) a polypeptide according to claim 1;
- (b) a polynucleotide according to claim 4;
- (c) an antibody according to any one of claims 11-13;
- 30 (d) a fusion protein according to claim 14; and

(e) a polynucleotide according to claim 18.

20. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- 5 (a) a polypeptide according to claim 1;  
(b) a polynucleotide according to claim 4;  
(c) an antibody according to any one of claims 11-13;  
(d) a fusion protein according to claim 14; and  
(e) a polynucleotide according to claim 18.

10

21. A vaccine according to claim 20, wherein the immunostimulant is an adjuvant.

22. A vaccine according to claim 20, wherein the immunostimulant  
15 induces a predominantly Type I response.

23. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 19.

20

24. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

25. A pharmaceutical composition comprising an antigen-presenting cell  
25 that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

26. A pharmaceutical composition according to claim 25, wherein the antigen presenting cell is a dendritic cell or a macrophage.

27. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.
- 5 28. A vaccine according to claim 27, wherein the immunostimulant is an adjuvant.
29. A vaccine according to claim 27, wherein the immunostimulant induces a predominantly Type I response.
- 10 30. A vaccine according to claim 27, wherein the antigen-presenting cell is a dendritic cell.
31. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, and thereby inhibiting the development of a cancer in the patient.
- 15 32. A method according to claim 31, wherein the antigen-presenting cell is a dendritic cell.
- 20 33. A method according to any one of claims 23, 24 and 31, wherein the cancer is prostate cancer.
- 25 34. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- 30



(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

5 wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate-specific protein from the sample.

35. A method according to claim 34, wherein the biological sample is  
10 blood or a fraction thereof.

36. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

15

37. A method for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;

20 (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); and

(iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii),  
25 under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

38. An isolated T cell population, comprising T cells prepared according to the method of claim 37.

30

39. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 38.

5 40. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

- (i) a polypeptide according to claim 1;
- 10 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;
- (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
- 15 (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

20

41. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

- 25 (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;
- 30 (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

5 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

42. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

10 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

20 (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

43. A method according to claim 42, wherein the binding agent is an antibody.

25

44. A method according to claim 43, wherein the antibody is a monoclonal antibody.

45. A method according to claim 42, wherein the cancer is prostate cancer.

30

46. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- 5 (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;
- 10 (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the  
15 amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

47. A method according to claim 46, wherein the binding agent is an antibody.

20

48. A method according to claim 47, wherein the antibody is a monoclonal antibody.

49. A method according to claim 46, wherein the cancer is a prostate  
25 cancer.

50. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with an  
30 oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein,

wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

5 (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

10

51. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15

52. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

53. A method for monitoring the progression of a cancer in a patient,  
20 comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315,  
25 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from  
30 the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

5                    54. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

10                   55. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

                    56. A diagnostic kit, comprising:  
                    (a) one or more antibodies according to claim 11; and  
15                   (b) a detection reagent comprising a reporter group.

                    57. A kit according to claim 56, wherein the antibodies are immobilized on a solid support.

20                   58. A kit according to claim 56, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

                    59. A kit according to claim 56, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups,  
25                   enzymes, biotin and dye particles.

                    60. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is  
30                   encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45,

47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides.

61. A oligonucleotide according to claim 60, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536.

15

62. A diagnostic kit, comprising:

(a) an oligonucleotide according to claim 61; and

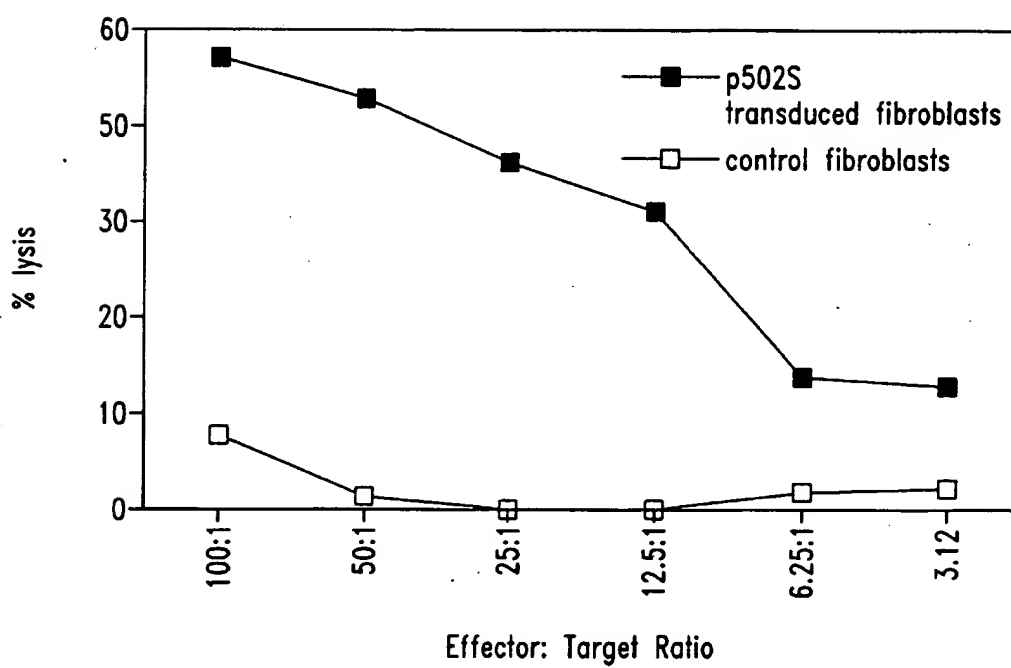
(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

20

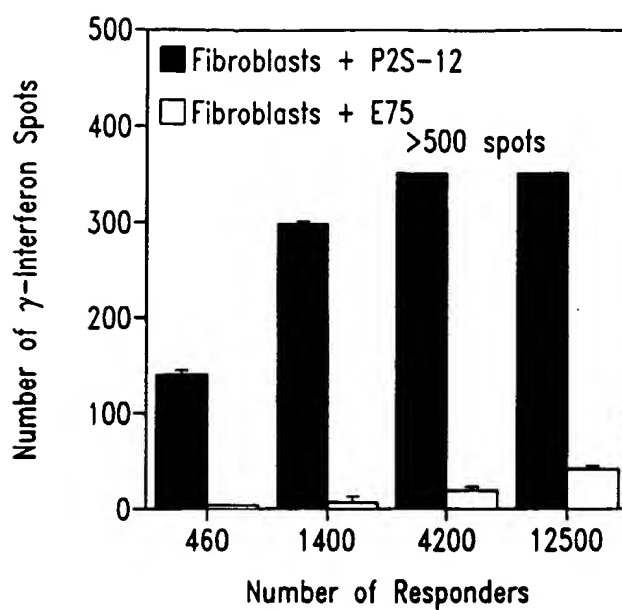
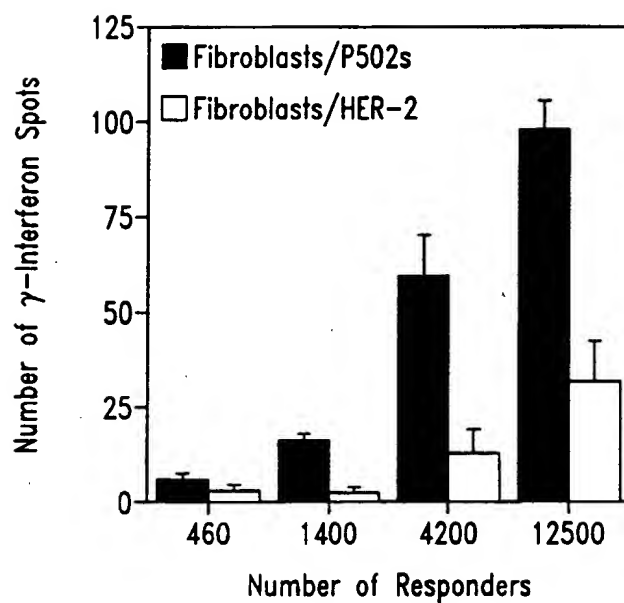
63. A host cell according to claim 10, wherein the cell is selected from the group consisting of: *E. coli*, baculovirus and mammalian cells.

64. A recombinant protein produced by a host cell according to claim 10.

25

*Fig. 1*



*Fig. 2A**Fig. 2B*

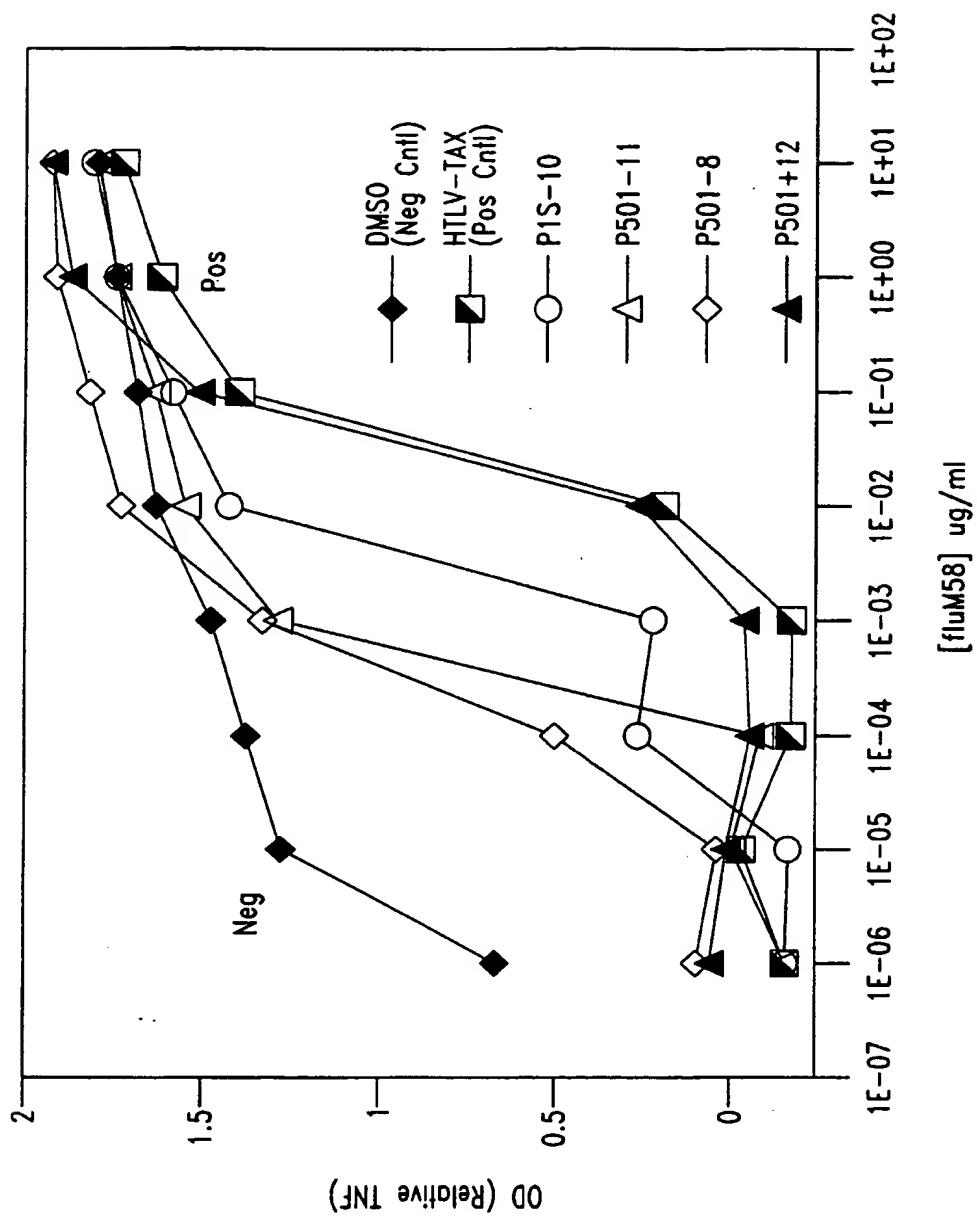
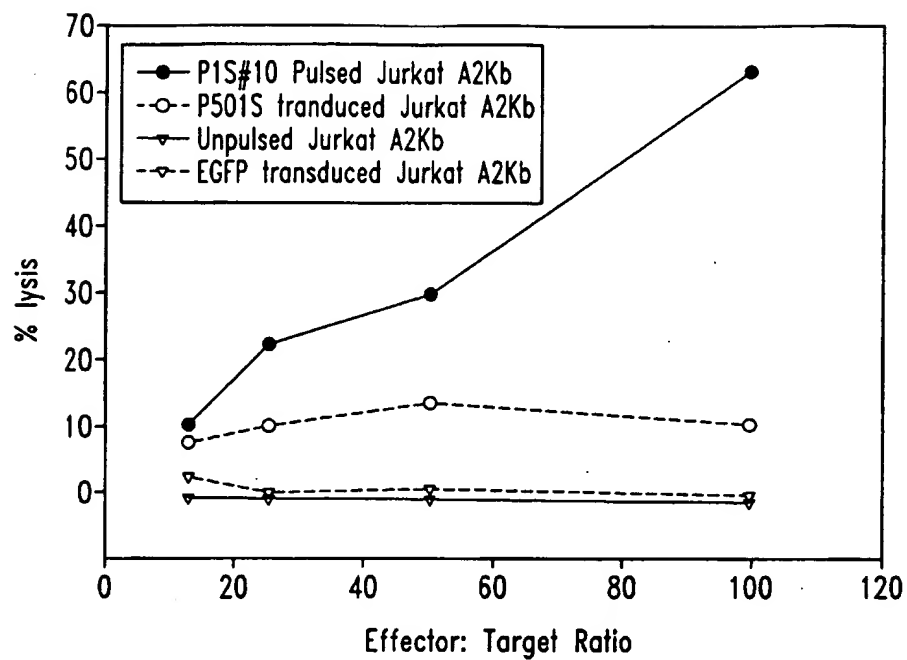
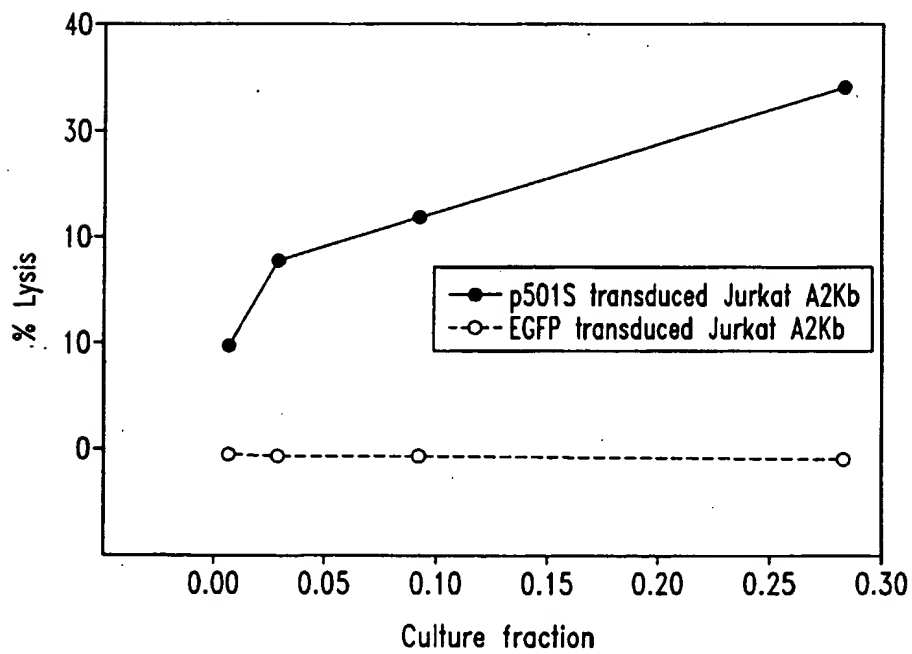
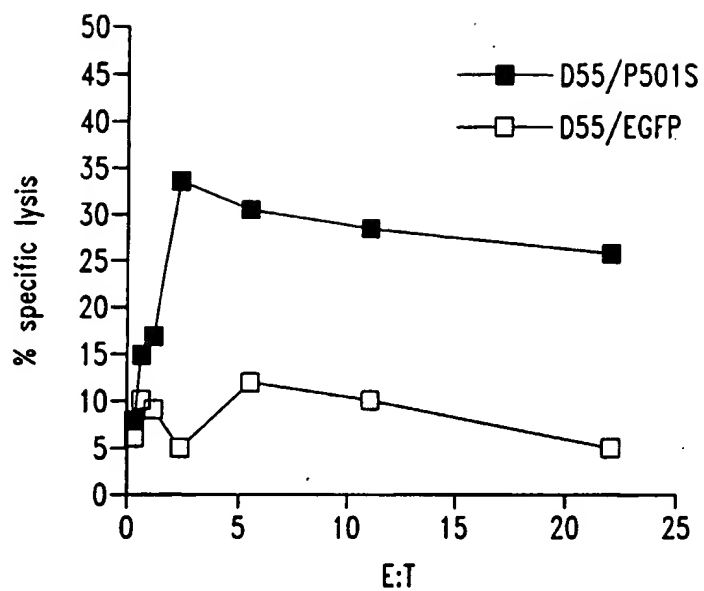
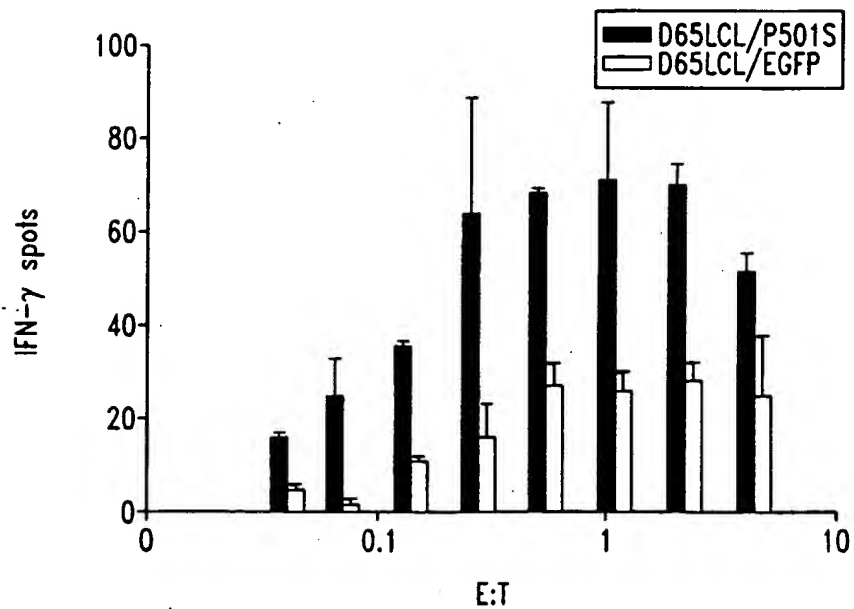
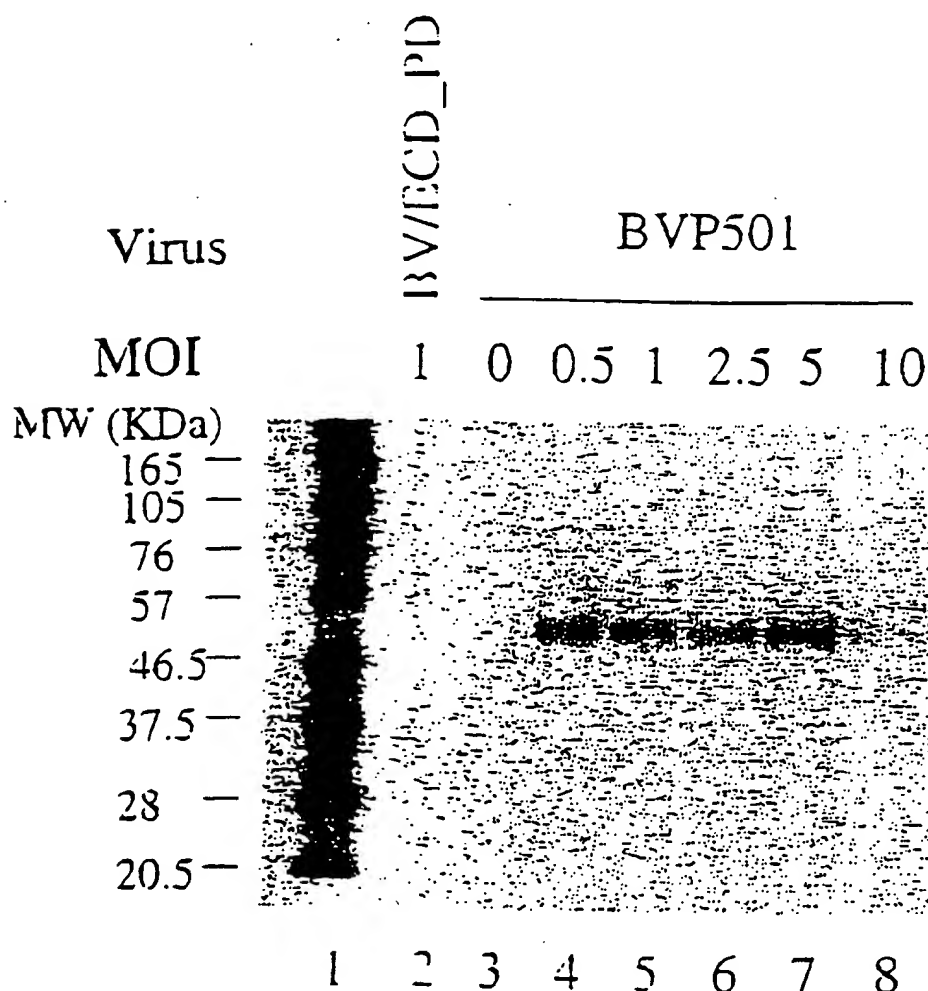


Fig. 3

*Fig. 4**Fig. 5*

*Fig. 6A**Fig. 6B*

# Expression of P501S by the Baculovirus Expression System



0.6 million high 5 cells in 6-well plate were infected with an unrelated control virus BV/ECD\_PD (lane 2), without virus (lane 3), or with recombinant baculovirus for P501 at different MOIs (lane 4 - 8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

Fig. 7



Schematic of P501S with predicted  
transmembrane, cytoplasmic, and extracellular regions

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 HQLCCRMPRTLRR LFVAELCSWMALMTFTLFYTDF VEGLYQQVPRAEPGTEARRHYDEGVR  
MGSLGLFLQCAISLVFSLVM DRLVQRFGTRAVYLAS VAAFVAAAGATCLSHSVAVVTA SAA  
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 LPPPPALCGASACDVSVRVVVGEPTEARVVPGRG ICLDLAILDSAFLLSQVAPSLF MGSIVQLSQS  
 VTAYMVSAAGLGLVAIYFAT QVVFDKSDLAKYSA

Underlined sequence: Predicted transmembrane domain; Bold sequence:  
 Predicted extracellular domain; *Italic sequence*: Predicted intracellular  
 domain. Sequence in bold/underlined: used generate polyclonal rabbit  
 serum

Localization of domains predicted using HMMTOP (G.E. Tusnady and I. Simon  
 (1998) Principles Governing Amino Acid Composition of Integral Membrane  
 Proteins: Applications to topology Prediction. J. Mol. Biol. 283, 489-506.

*Fig. 9*

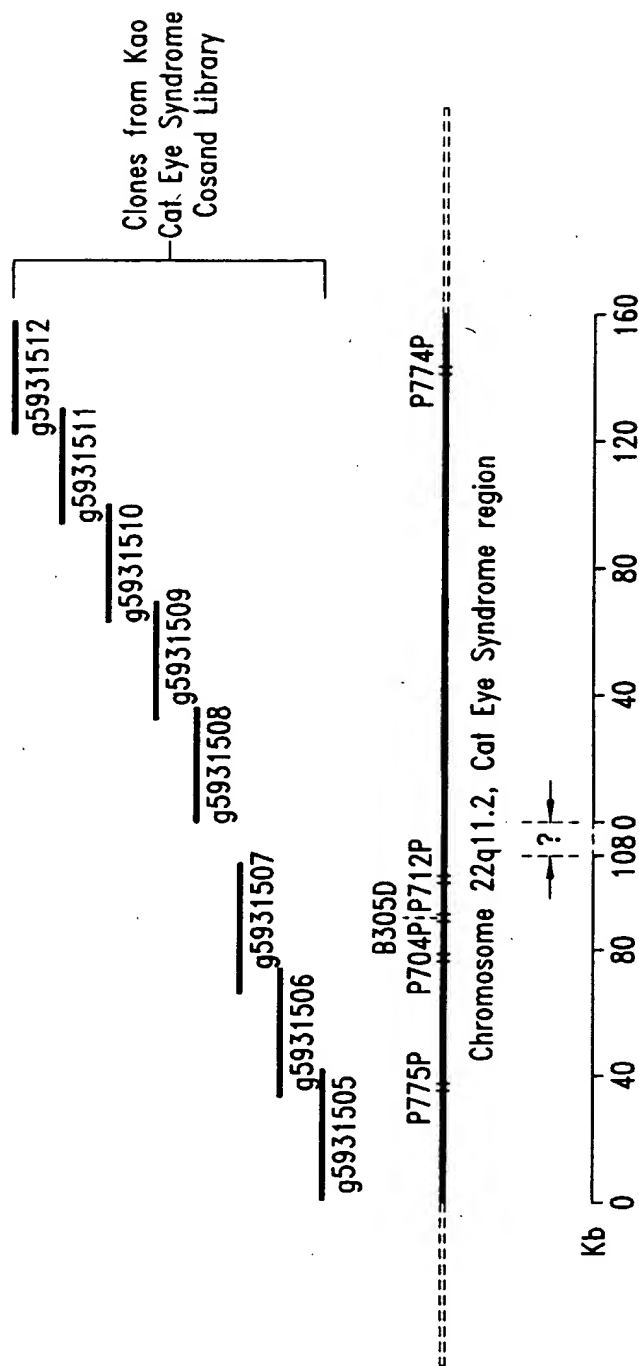


Fig. 10



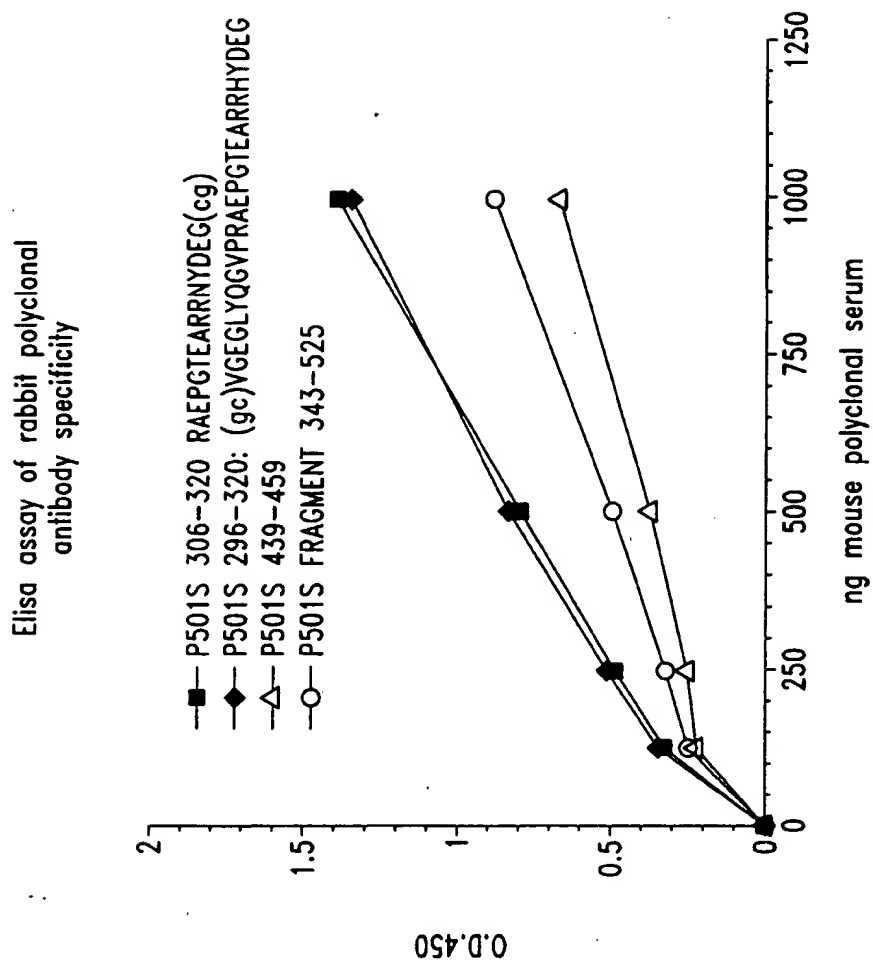


Fig. 11

## SEQUENCE LISTING

<110> Corixa Corporation  
 Xu, Jiangchun  
 Dillon, Davin C.  
 Mitcham, Jennifer L.  
 Harlocker, Susan Louise  
 Jiang Yuqui  
 Reed, Steven G.  
 Kalos, Michael  
 Fanger, Gary  
 Retter, Mark  
 Solk, John  
 Day, Craig  
 Skeiky, Yasir A.W.  
 Wang, Aijun

<120> COMPOSITIONS AND METHODS FOR THE THERAPY AND  
 DIAGNOSIS OF PROSTATE CANCER

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&lt;211&gt; 818

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)... (818)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 6

tttttttttt	tttttttttt	aagaccctca	tcaatagatg	gagacataca	gaaatagtca	60
aaccacatct	acaaaatgcc	agtatcaggc	ggcggtctcg	aagccaaagt	gatgtttgga	120
tgtaagaatga	aatattagtt	ggcgatgaa	gcagatagtg	aggaaagttg	agccaataat	180
gacgtgaagt	ccgtggaagc	ctgtggctac	aaaaaatgtt	gagccgtaga	tgccgtcgga	240
aatggtgaag	ggagactcga	agtactctga	ggcttgtagg	agggtaaaat	agagaccag	300

taaaattgta	ataagcagtg	cttgaattat	ttggtttcgg	ttgtttttcta	ttagactatg	360
gtgagctcag	gtgattgata	ctcctgatgc	gagtaatacg	gatgtgttta	ggagtggggac	420
ttctagggga	tttagcgggg	tgatgcctgt	tggggggccag	tgccctccta	gttgggggggt	480
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ggtaataaat	aggattatcc	cgtatcgaag	gccttttttg	acaggtgggtg	tgtgtgtggcc	600
ttgggtatgtg	ctttctcgtg	ttacatcgcg	ccatcattgg	tatatgggta	gtgtgttggg	660
ttantangg	ctantatgaa	gaacttttgg	antggaatta	aatcaatngc	ttggccggaa	720
gtcattanga	nggctnaaaa	ggccctgtta	ngggctctggg	ctnggtttta	cccnacccat	780
ggaatncnc	ccccggacna	ntgnatccct	attcttaa			818

&lt;210&gt; 7

&lt;211&gt; 817

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (817)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 7

tttttttttt	tttttttttt	tggtctctaga	gggggtagag	gggggtgctat	agggtaaata	60
cgggccctat	ttcaaagatt	tttaggggaa	ttaattctag	gacgatgggt	atgaaactgt	120
ggtttgctcc	acagatttca	gagcattgac	cgtagtatac	ccccggtcgt	gtagcgggtga	180
aagtggtttg	gttttagacgt	ccgggaattg	catctgtttt	taagcctaata	gtggggacag	240
ctcatgagtg	caagacgtct	tgtgatgtaa	ttattatacn	aatgggggct	tcaatcggga	300
gtactactcg	attgtcaacg	tcaaggagtc	gcaggtcgcc	tggttctagg	aataatgggg	360
gaagtatgta	ggaattgaag	attaatccgc	cgtagtcggg	gttctcctag	gttcaatacc	420
attgggtggc	aattgatttg	atggtaaggg	gagggatcgt	tgaactcgtc	tggtatgtaa	480
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gaatnttnng	gaaaagggct	tacaggacta	gaaaccaaata	angaaaanta	atnntaangg	660
cnttatcntn	aaaggtgnata	accnctccta	tnatcccacc	caatngnatt	ccccacncnn	720
acnattggat	ccccanttc	canaaanggc	cnccccccg	tgnannccnc	cttttgttcc	780
cttnantgan	gggtattcnc	ccctngcntt	atcanc			817

&lt;210&gt; 8

&lt;211&gt; 799

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (799)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 8

catttccggg	tttactttct	aaggaaagcc	gagcgggaagc	tgctaacgtg	ggaatcgggtg	60
cataaggaga	actttctgct	ggcacgcgct	agggacaagc	gggagagcga	ctccgagcgt	120
ctgaagcgca	cgccccagaa	gggtggacttg	gcactgaaac	agctgggaca	catccgcgag	180
tacgaacagc	gcctgaaagt	gctggagcgg	gaggtccagc	agtgtagccg	cgctcctggg	240
tgggtggccg	angcctganc	cgctctgctt	tgctgcccc	angtgggccc	ccaccccttg	300
acctgcctgg	gtccaaacac	tgagccctgc	tggcggactt	caagganaac	ccccacangg	360
ggattttgct	cctanantaa	ggctcatctg	ggcctcggcc	ccccacctg	gttggccttg	420
tctttgangt	gagccccatg	tccatctggg	ccactgtcng	gaccaccttt	ngggagtgtt	480
ctccttacia	ccacannatg	cccggctcct	cccggaaacc	antcccance	tgngaaggat	540
caagnccctg	atccactnnt	nctanaaccg	gcncncncg	cngtggaaac	cnccttntgt	600
tccttttctt	tnagggttaa	tnnccgcttg	gccttnccan	ngtcctncnc	nttttccnnt	660

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gttnaaattg ttangcnccc nccnntcccn cnnncnnan cccgaccnnc annttnnann 720
ncctgggggt nccnnngat tgaccnnc nccctntant tgcnttnggg nncnntgccc 780
ctttccctct nggganncg 799

```

```

<210> 9
<211> 801
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G

```

```

<400> 9
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caaggacaag gccaccaggt gcgggggccc aagcccacat gatccttact ctatgagcaa 180
aatccctgtt gggggcttct ccttgaagtc cggcancagg gctcagttct tggacccang 240
caggtcatgg ggttgtngnc caactggggg ccncaacgca aaanggcncg gggcctcngn 300
caccatccc angacgcggc tacactnctg gacctccnc tccaccactt tcatgcgctg 360
ttcntaccg cgnatntgtc ccantgttt cngtgccnac tccancttct nggacgtgcg 420
ctacatacgc ccggantenc nctcccgtt tgtccctatc cagtnccan caacaaattt 480
cncntantg caccnattcc cacntttnc agntttccnc nncngcttc cttntaaaag 540
ggttganccc cggaaaatnc ccaaagggg gggggccngg tacccaactn cccctnata 600
gctgaantcc ccatnaccnn gncctnatgg anccntcent ttttaannacn ttctnaactt 660
gggaanance ctcgncntn ccccnttaa tccnccttg cnangnnent ccccnntcc 720
nccnnntng gcntntnann cnaaaaaggc ccnnnancaa tctcctnnen cctcanttcg 780
ccanccctcg aaatcggccn c 801

```

```

<210> 10
<211> 789
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(789)
<223> n = A,T,C or G

```

```

<400> 10
cagtctatnt ggccagtgtg gcagctttcc ctgtggetgc cggtgccaca tgectgtccc 60
acagtgtggc cgtggtgaca gcttcagccg ccctcaccgg gttcaccttc tcagccctgc 120
agatcctgdc ctacacactg gcctccctct accaccggga gaagcagggtg ttcctgccc 180
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttcctgc 240
caggccctaa gcctggagct cccttcctta atggacacgt ggggtgctgga ggcagtggcc 300
tgctcccacc tccaccgcy ctctgcgggg cctctgcttg tgatgtctcc gtacgtgtgg 360
tggtgggtga gccaccgan gccagggtgg ttccggggcg gggcatctgc ctggacctcg 420
ccatcctgga tagtgcttcc tgetgtccca ngtgggccca tccctgttta tgggtccat 480
tgtccagctc agccagtctg tcaactgcta tatggtgtct gccgcaggcc tgggtctggt 540
cccatttact ttgctacaca ggtantattt gacaagaacg anttgccaa atactcagcg 600
ttaaaaaatt ccagcaacat tgggggtgga aggcctgcct cactgggtcc aactccccgc 660
tcctgttaac cccatggggc tgccggcttg gccgccaatt tctgttgctg ccaaantnat 720
gtggtctctc gctgccacct gttgctggct gaagtgcnta cngcncanct nggggggtng 780
gngttccc 789

```

```

<210> 11
<211> 772

```

<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(772)  
<223> n = A,T,C or G

<400> 11

cccaccctac	ccaaatatta	gacaccaaca	cagaaaagct	agcaatggat	tcccttctac	60
tttgttaaat	aaataagtta	aatatattaaa	tgcctgtgtc	tctgtgatgg	caacagaagg	120
accaacaggg	cacatcctga	taaaaggtaa	gaggggggtg	gatcagcaaa	aagacagtgc	180
tgtgggctga	ggggacctgg	ttcttgtgtg	ttgcccctca	ggactcttcc	cctacaaata	240
actttcatat	gttcaaatcc	catggaggag	tgtttcatcc	tagaaactcc	catgcaagag	300
ctacattaaa	cgaagctgca	ggttaagggg	cttanagatg	ggaaaccagg	tgactgagtt	360
tattcagctc	ccaaaaaccc	ttctctaggt	gtgtctcaac	taggaggcta	gctgttaacc	420
ctgagcctgg	gtaatccacc	tgcagagtcc	ccgcattcca	gtgcatggaa	cccttctggc	480
ctccctgtat	aagtccagac	tgaaccccc	ttggaaggnc	tccagtcagg	cagccctana	540
aactggggaa	aaaagaaaa	gacgccccan	ccccagctg	tgcantctacg	cacctcaaca	600
gcacaggggtg	gcagcaaaaa	aaccacttta	ctttggcaca	aacaaaaaact	ngggggggca	660
accccggcac	cccnangggg	gttaacagga	ancngggnaa	cntggaaccc	aattnaggca	720
ggcccncac	ccnaatntt	gctgggaaat	tttctctccc	ctaaattntt	tc	772

<210> 12  
<211> 751  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(751)  
<223> n = A,T,C or G

<400> 12

gccccaatte	cagctgccac	accacccacg	gtgactgcat	tagttcggat	gtcatacaaa	60
agctgattga	agcaaccctc	tacttttttg	tcgtgagcct	tttgccttgg	gcaggtttca	120
ttggctgtgt	tggtgacgtt	gtcattgcaa	cagaatgggg	gaaaggcact	gttctctttg	180
aagtanggtg	agtcctcaaa	atccgtatag	ttgggtgaagc	cacagcactt	gagccctttc	240
atgggtgtgt	tccacacttg	agtgaagtct	tccctgggaac	cataatcttt	cttgatggca	300
ggcactacca	gcaacgtcag	ggaagtgtc	agccattgtg	gtgtacacca	aggcgaccac	360
agcagctgcn	acctcagcaa	tgaagatgan	gaggangatg	aagaagaacg	tcncgagggc	420
acacttgctc	tcagtcttan	caccatanca	gcccntgaaa	accaananca	aagaccacna	480
cnccggctgc	gatgaagaaa	tnaccccneg	ttgacaaact	tgcatggcac	tggganccac	540
agtggcccna	aaaatcttca	aaaaggatgc	cccactnatt	gaccccccaa	atgccacttg	600
ccaacagggg	ctgccccacn	cncnnaacga	tgancnatt	gnacaagatc	tncntggtct	660
tnatnaacnt	gaacctgtcn	tngtggctcc	tgttcaggnc	cnnggcctga	cttctnaann	720
aangaactcn	gaagncacca	cngganannc	g			751

<210> 13  
<211> 729  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(729)  
<223> n = A,T,C or G

## &lt;400&gt; 13

gagccaggcg	tccctctgcc	tgcccactca	gtggcaacac	ccgggagctg	ttttgtcctt	60
tgtggancct	cagcagtncc	ctctttcaga	actcantgcc	aaganccctg	aacaggagcc	120
accatgcagt	gcttcagctt	cattaagacc	atgatgatcc	tcttcaattt	gtcatctttt	180
ctgtgtggtg	cagccctggt	ggcagtgggc	atctgggtgt	caatcgatgg	ggcatccttt	240
ctgaagatct	tcggggccact	gtcgtccagt	gccatgcagt	ttgtcaacgt	gggctacttc	300
ctcatcgtag	ccggcggtgt	ggctcttagct	ctagggtttcc	tgggctgcta	tgggtgctaag	360
actgagagca	agtgtgccct	cgtgacgttc	ttcttcatcc	tcctcctcat	cttcattgct	420
gaggttgcaa	tgtgtgggtc	gccttggtgt	acaccacaat	ggctgagcac	ttcctgacgt	480
tgtgtgtaat	gcctgccatc	aanaaaagat	tatgggttcc	caggaanact	tactcaagt	540
gttgaacac	caccatgaaa	gggtcaagt	gctgtggctt	cnnccaacta	tacggatttt	600
gaagantcac	ctacttcaaa	gaaaanagt	cctttccccc	atttctgttg	caattgacaa	660
acgtcccaa	cacagccaat	tgaaaacctg	cacccaaccc	aaanggttcc	ccaaccanaa	720
attnaagg						729

&lt;210&gt; 14

&lt;211&gt; 816

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (816)

&lt;223&gt; n = A,T,C or G

## &lt;400&gt; 14

tgtcttctct	caaagttggt	cttgttgcca	taacaaccac	cataggtaaa	gcgggagcag	60
tgttcgtgta	aggggttgta	gtaccagcgc	gggatgctct	ccttgagag	tcctgtgtct	120
ggcaggtcca	cgcagtgcc	tttgtcactg	gggaaatgga	tgcgtggag	ctcgtcaaag	180
ccactcgtgt	atttttcaca	ggcagcctcg	tccgacgcgt	cggggcagtt	gggggtgtct	240
tcacactcca	ggaaactgtc	natgcagcag	ccattgctgc	agcggaaactg	gggtgggtgta	300
cangtgccag	agcacactgg	atggcgctt	tccatgnnan	gggccctgng	ggaaagtccc	360
tgancccan	anctgcctct	caaangcccc	accttgacac	ccccgacagg	ctagaatgga	420
atcttcttcc	cgaaggttag	ttnttcttgt	tgcccaancc	anccccntaa	acaaactctt	480
gcanatctgc	tccngggggg	tcntantacc	ancgtgggaa	aagaacccca	ggcngcgaac	540
caancttgtt	tggatnecaa	gcnataatct	nctnttctgc	ttgggtggaca	gcaccantna	600
ctgtnnanct	ttagnccntg	gtcctcntgg	gttgnncttg	aacctaatcn	ccnntcaact	660
gggacaaggt	aantngccnt	ccttttaatt	cccnancntn	ccccctgggt	tgggggttttn	720
cncnctccta	ccccagaaan	nccgtgttcc	cccccaacta	ggggccnaaa	ccnnttnttc	780
cacaaccctn	ccccaccac	gggttcngnt	ggttng			816

&lt;210&gt; 15

&lt;211&gt; 783

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (783)

&lt;223&gt; n = A,T,C or G

## &lt;400&gt; 15

ccaaggcctg	ggcaggcata	nacttgaagg	tacaacccca	ggaaccctg	gtgctgaagg	60
atgtggaaaa	cacagattgg	cgctactgc	gggggtgacac	ggatgtcagg	gtagagagga	120
aagacccaaa	ccaggtggaa	ctgtggggac	tcaaggaang	cacctacctg	ttccagctga	180
cagtgcctag	ctcagaccac	ccagaggaca	cggccaacgt	cacagtcact	gtgctgtcca	240
ccaagcagac	agaagactac	tgcctcgcat	ccaacaangt	gggtcgctgc	cggggctctt	300
ttccacgctg	gtactatgac	cccacggagc	agatctgcaa	gagtttcgtt	tatggaggct	360



gcttgggcaa	caagaacaac	taccttcggg	aagaagagt	cattctancc	tgtcnggggtg	420
tgcaagggtg	gcctttgana	ngcanctctg	gggctcangc	gactttcccc	cagggccccc	480
ccatggaaag	gcgccatcca	ntgttctctg	gcacctgtca	gcccacccag	ttccgctgca	540
ncaatggctg	ctgcatcnac	antttcctng	aattgtgaca	acacccccca	ntgcccccaa	600
ccctcccaac	aaagcttccc	tgttnaaaaa	tacnccant	ggcttttnac	aaacncccg	660
cncctccntt	ttcccnntn	aacaaagggc	nctngcnttt	gaactgccc	naaccnngaa	720
tctnccnngg	aaaaantncc	ccccctggtt	cctnnaance	cctcncnaa	antncccccc	780
ccc						783

&lt;210&gt; 16

&lt;211&gt; 801

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(801)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 16

gccccaatc	cagctgccac	accacccacg	gtgactgcat	tagttcggat	gtcatacaaa	60
agctgattga	agcaaccctc	tacttttttg	tcgtgagcct	tttgcttgg	gcaggtttca	120
ttggctgtgt	tggtgacgtt	gtcattgcaa	cagaatgggg	gaaaggcact	gttctctttg	180
aagtaggggtg	agtcctcaaa	atccgtatag	ttggtgaagc	cacagcactt	gagccctttc	240
atgggtgggtg	tccacacttg	agtgaagtct	tcctgggaac	cataatcttt	cttgatggca	300
ggcactacca	gcaacgtcag	gaagtgtc	gccattgtgg	tgtacaccaa	ggcgaccaca	360
gcagctgcaa	cctcagcaat	gaagatgagg	aggaggatga	agaagaacgt	cncgagggca	420
cacttgctct	ccgtcttagc	accatagcag	cccangaaac	caagagcaaa	gaccacaacg	480
ccngctgcga	atgaaagaaa	ntacccacgt	tgacaaaactg	catggccact	ggacgacagt	540
tggcccgaan	atcttcagaa	aagggatgcc	ccatcgattg	aacacccana	tgcccactgc	600
cnacagggtg	gncncncn	gaaagaatga	gccattgaag	aaggatcntc	ntggctcttaa	660
tgaactgaaa	ccntgcatgg	tggcccctgt	tcagggtctc	tggcagtga	ttctganaaa	720
aaggaacngc	ntnagcccc	ccaaangana	aaacaccccc	gggtgttgcc	ctgaattggc	780
ggccaaggan	ccctgcccc	g				801

&lt;210&gt; 17

&lt;211&gt; 740

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(740)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 17

gtgagagcca	ggcgtccctc	tgcctgccca	ctcagtgcca	acacccggga	gctgttttgt	60
cctttgtgga	gcctcagcag	ttccctcttt	cagaactcac	tgccaagagc	cctgaacagg	120
agccaccatg	cagtgttca	gcttcattaa	gaccatgatg	atcctcttca	atttgctcat	180
ctttctgtgt	gggtgcagccc	tggtggcagt	gggcatctgg	gtgtcaatcg	atggggcatc	240
ctttctgaag	atcttcgggc	cactgtcgtc	cagtgccatg	cagtttgtca	acgtgggcta	300
cttcctcatc	gcagccggcg	ttgtggctct	tgtcttgggt	ttcctgggct	gctatgggtg	360
taagacggag	agcaagtgtg	ccctcgtgac	gttctctctc	atcctctctc	tcactcttcat	420
tgtggaagtt	gcagctgctg	tggtcgcctt	gggtgtacac	acaatggctg	aaccattcct	480
gacgttgctg	gtantgcctg	ccatcaanaa	agattatggg	ttcccaggaa	aaattcactc	540
aantntggaa	caccnccatg	aaaagggctc	caatttctgn	tggttcccc	aactataccg	600
gaattttgaa	agantcnccc	tacttccaaa	aaaaaanant	tgcttttnc	ccenttctgt	660
tgcaatgaaa	acntcccaan	acngccaatn	aaaacctgcc	cnnncaaaaa	ggntcncaaa	720

caaaaaaant nnaagggttn

740

<210> 18  
 <211> 802  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(802)  
 <223> n = A,T,C or G

<400> 18  
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 caaggtcttc cagctgccgc acattacgca gggcaagagc ctccagcaac actgcatatg 120  
 ggatacactt tacttttagca gccagggtga caactgagag gtgtcgaagc ttattcttct 180  
 gagcctctgt tagtggagga agattccggg cttcagctaa gtagtcagcg tatgtcccat 240  
 aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa 300  
 cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat 360  
 ggatgagtgt ggcagcgtt gccccttgg ccgacttggc taggagcaga aattgctcct 420  
 ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg 480  
 gctcaggatg tccagagacg tggttccgcc ccctcnctta atgacaccgn ccanncaacc 540  
 gtcggctccc gccgantgng ttcgtcgtnc ctgggtcagg gtctgctggc cncacttgc 600  
 aancctcgtc nggcccattg aattcaccnc accggaactn gtangatcca ctntttctat 660  
 aaccggnccg caccgcnnnt ggaactccac tcttntncc tttacttgag ggtaagggtc 720  
 acccttnnccg ttaccttggg ccaaaccntn cntgtgtcg anatngtnaa tcnggnccna 780  
 tnccanccnc atangaagcc ng 802

<210> 19  
 <211> 731  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(731)  
 <223> n = A,T,C or G

<400> 19  
 cnaagcttcc aggtnacggg ccgcnaance tgaccnagg tancanaang cagnccgcgg 60  
 gagcccaccg tcacngngng gngtctttat nggagggggc ggagccacat cncctggacnt 120  
 cntgacccca actccccncc ncncantgca gtgatgagtg cagaactgaa ggtnacgtgg 180  
 caggaaccga gancaaannc tgctccnntc caagtccgcn nagggggcgg ggctggccac 240  
 gncatccnt cnaagtgtgn aaagccccnn cctgtctact tgtttgaga acngcnnga 300  
 catgccagn gttanataac nggcnagag tnannttgcc tctcccttcc ggctgcgcan 360  
 cngntntgct tagnggacat aacctgacta cttaactgaa ccnngaate tnccnccct 420  
 ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta 480  
 aagtgtaccc catncccaat gtntgctnga ngctctgnc tgcnttangt tcggtcctgg 540  
 gaaagacctat caattnaagc tatgtttctg actgcctctt gtcacctgna acaancnacc 600  
 cncnntcca aggggggnc ggccccaat ccccccaacc ntnaattnan ttancccn 660  
 cccccnggcc cggcctttta cnancntenn nnacngggna aaaccnnngc ttncccaac 720  
 nnaatccncc t 731

<210> 20  
 <211> 754  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(754)  
 <223> n = A,T,C or G

<400> 20  
 . tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60  
 caaccccctc ntccaaatnn ccntttccgg gnggggggttc caaacccaan ttanntttgg 120  
 annttaaatt aaatnttntt tggngggnna anccnaatgt nangaaagtt naaccanta 180  
 tnancttnaa tncctggaaa ccngtngntt ccaaaaatnt ttaaccctta antccctccg 240  
 aaatngttna nggaaaaccc aanttctcnt aagggtgttt gaaggntnaa tnaaaanccc 300  
 nnccaattgt ttttngccac gcctgaatta attggnnttc gntgttttcc nttaaaanaa 360  
 ggnnancccc ggttantnaa tcccccnnc cccaattata ccganttttt ttngaattgg 420  
 gancccnccg gaattaacgg ggnnnntccc tnttgggggg cnggnncccc cccntcggg 480  
 ggttngggnc aggnncnaat tgtttaagg tccgaaaaat ccctccnaga aaaaaanctc 540  
 ccaggntgag nntnggggtt ncccccccc canggccct ctcgnanagt tgggggttgg 600  
 ggggcctggg attttntttc cctntttnc tcccccccc ccnggganag aggttngngt 660  
 tttgntcnnc ggcccnccn aagancttn cganttnan ttaaattcnt gcctnggcga 720  
 agtcnttgn agggntaaan ggccccctnn cggg 754

<210> 21  
 <211> 755  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(755)  
 <223> n = A,T,C or G

<400> 21  
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 nncanattcc actganngcg cganngngan ngagaaanct nataccanag ncaccanacn 180  
 ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattn 240  
 nncnncanac gattttcctn anccgattac ccntncccc tanccctcc cccccaacna 300  
 cgaaggcnct ggncnaagg nngcgncc cgcgtagntc ccnncnaagt cncncncta 360  
 aactcancn nattacnccg ttcttgagta tctctcccg aatctcacc tactcaactc 420  
 aaaaanacn gatacaaaat aatncaagc tgnattatnac actntgactg ggtctctatt 480  
 ttagnggtcc ntnaancntc ctaatacttc cagtctnct tcnccaattt ccnaangget 540  
 ctttcngaca gcatntttt gttcccnntt ggggtcttan ngaattgccc ttctntgaac 600  
 gggctcntct tttccttcgg ttancctggg ttcnncggc cagttattat ttccntttt 660  
 aaattcntnc cntttanttt tggcnttcna aacccccggc cttgaaaacg gccccctgg 720  
 aaaagggtgt tttganaaaa tttttgtttt gttcc 755

<210> 22  
 <211> 849  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(849)  
 <223> n = A,T,C or G

<400> 22  
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 acgctnggan taangcgacc cganttttag gannccct aaaatcanac tgtgaagatn 120

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atcctgnnna cggaanggtc accggnggat nntgctaggg tgnccnctcc cannnenttn 180
cataactcng nggcctgcc caccaccttc ggcgcceng ngcccgggcc cgggtcattn 240
gnnttaaccn cactnngcna ncggtttccn nccccnng acccnggcga tccggggtn 300
tctgtcttcc cctgnagncn anaaantggg ccncggncce ctttaccct nnacaagcca 360
cngcctteta nccnngccc cccctccant nngggggact gccnanngt ccgttntng 420
nnaccccnnn gggtnccctg gttgtcgant cnaccgnang ccanggatc cnaaggaagg 480
tgcgttnttg gcccctacc ttcgctnccg nncaccttc ccgacnanga nccgtcccg 540
cncnncgng cctcncctcg caacacccgc nctcntngt ncggnnccc cccacccgc 600
nccctcnenc ngncgnancn ctcnccncc gtctcannca ccaccccgcc ccgccaggcc 660
ntcanccacn ggngacnng nagnccntc gncgcgcgn gcgncnccet cgcncngaa 720
ctnctcngg ccantnncgc tcaancnna cnaaacgcg ctgcgcggcc cgnagcgnc 780
ncctcncga gtcctcccg cttccnacc angnttccn cgaggacacn nnaccccgcc 840
nncangcgg

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<210> 23

<211> 872

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (872)

<223> n = A,T,C or G

<400> 23

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gcgcaacta tactcgctc gnactcgtgc gcctcgctnc tcttttctc cgcaaccatg 60
tctgacnanc ccgattnggc ngatatchan aagntcganc agtccaaact gantaacaca 120
cacacnancn aganaaatcc nctgccttcc anagtanacn attgaacnng agaaccangc 180
nggcgaatcg taatnaggcg tgcgcgcgcca atntgtcncc gtttattntn ccagcntcnc 240
ctnccnacc tacntcttcn nagctgtcnn acccctngtn cgnaccccc naggtcgga 300
tcgggtttnn nntgaccgng cnnccctcc cccntccat nacganccnc ccgcaccacc 360
nanngcncgc nccccgnct cttegcncnc ctgtcctntn cccctgtngc ctggcncngn 420
accgcattga cctcgccnn ctncnngaaa ncgnanacgt ccgggttggn annancgctg 480
tgggnnngcg tctgncgcg gttccttcn ncncttcca ccattctct tacngggct 540
ccnccctc tcnncacnc cctgggacgc tntcctntgc ccccttnac tccccctt 600
cgcgtgncc cgncccccacc ntcatttnca nacgntcttc acaannccet ggntnnctcc 660
cnancnngcn gtcancnag ggaagggngg ggnccnntg nttgacgttg ngngangtc 720
cgaanantcc tcnccntcan cncctaccct cggcggnct ctngttncc aacttancaa 780
ntctcccccg ngngcnctc tcagcctcnc cnccccnct ctctgcantg tncctctgctc 840
tnaccnntac gantnttcgn cncctcttt cc 872

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<210> 24

<211> 815

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (815)

<223> n = A,T,C or G

<400> 24

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gcatgcaagc ttgagtattc tatagngtca cctaaatanc ttggcntaat catggctnta 60
nctgntctcc tgtgtcaaat gtatacnaa tanatatgaa tctnatntga caaganngta 120
tcntncatta gtaacaantg tntgtccat cctgtengan canattccca tnnattncgn 180
cgcattcn cnancantatn taatngggaa ncnntnnnn ncaccnccat ctatcntncc 240
gcnccctgac tggagagat ggatnanttc tntntgacc nacatgttca tcttgattn 300
aanaccccc cgcngnccac cgggtngng cnagccntc ccaagacctc ctgtggagg 360

```

aacctgcgtc	aganncatca	aacntgggaa	acccgcnncc	angtnnaagt	ngnnncanan	420
gatcccgtcc	aggnttnacc	atcccttcnc	agcgccecc	ttngtgcctt	anagnnagc	480
gtgtccnanc	cnetcaacat	ganacgcgcc	agnccanceg	caattnggca	caatgtcgnc	540
gaaccccccta	gggggantna	tncaaanccc	caggattgtc	cncncangaa	atcccnccanc	600
cccnccctac	ccncttttgg	gacngtgacc	aantcccgga	gtncaggtcc	ggccngnctc	660
ccccaccggt	nncntggggg	gggtgaanct	cngnntcanc	cngncgaggn	ntcgnaagga	720
accggncctn	ggncgaanng	ancnntcnga	agngccnct	cgtataaccc	cccctcncca	780
nccnacngnt	agntcccccc	cngggtncgg	aangg			815

&lt;210&gt; 25

&lt;211&gt; 775

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(775)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 25

ccgagatgtc	tcgctccgtg	gccttagctg	tgctcgcgct	actctctctt	tctggcctgg	60
aggctatcca	gcgtactcca	aagattcagg	tttactcacg	tcattccagca	gagaatggaa	120
agtcaaattt	cctgaattgc	tatgtgtctg	ggtttcatcc	atccgacatt	gaanttgcact	180
tactgaagaa	tggaanagaga	attgaaaaag	tgagacattc	agacttgtct	ttcagcaagg	240
actggctctt	ctatctctng	tactacactg	aattcacccc	cactgaaaaa	gatgagtatg	300
cctgccgtgt	gaaccatgtg	actttgtcac	agcccaagat	agttaagtgg	gatcgagaca	360
tgtaagcagn	cnncatggaa	gtttgaagat	gccgcatttg	gattggatga	attccaaatt	420
ctgcttgctt	gcnttttaat	antgatatgc	ntatacaccc	taccctttat	gncccccatt	480
tgtaggggtt	acatnantgt	tcnctnngga	catgatcttc	ctttataant	ccnccnttcg	540
aattgcccg	cnccnngttn	ngaattgttc	cnnaaccacg	gttggctccc	ccaggtcncc	600
tcttacggaa	gggcctgggc	cnctttncaa	ggttggggga	accnaaaatt	tcncttntgc	660
cncccncca	cnntcttng	nncncanttt	ggaacccttc	cnattccctt	tggcctcnna	720
nccttnncta	anaaaacttn	aaancgtngc	naaanntttn	acttcccccc	ttacc	775

&lt;210&gt; 26

&lt;211&gt; 820

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(820)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 26

anattantac	agtgtaatct	tttcccagag	gtgtgtanag	ggaacggggc	ctagaggcat	60
cccanaagata	ncttatanca	acagtgcctt	gaccaagagc	tgctgggcac	atttcctgca	120
gaaaagggtg	cggcccccat	cactcctcct	ctcccatagc	catcccagag	gggtgagtag	180
ccatcangcc	ttcgggtggg	gggagtcang	gaaacaacan	accacagagc	anacagacca	240
ntgatgacca	tgggcgggag	cgagcctctt	ccctgnaccg	gggtggcana	nganagccta	300
nctgaggggt	cacactataa	acgttaacga	ccnagatnan	cacctgcttc	aagtgcaccc	360
ttctacactg	acnaccagng	accnnnaact	gcngcctggg	gacagcnctg	ggancagcta	420
acnnagcact	cacctgcccc	cccatggccg	tnccgntccc	tggtcctgnc	aaggggaagct	480
ccctgttgga	attncggggg	naccaaggga	nccccctcct	ccanctgtga	aggaaaaann	540
gatggaattt	tncccttcgg	gcccntcccc	tcttctttta	cacgccccct	nntactcttc	600
tccctctntt	ntcctgnenc	acttttnacc	ccnnnatctt	ccttnattga	tcggannctn	660
ganattccac	tnncgcctnc	cntcnatcng	naanacnaaa	nactntctna	cccnggggat	720
gggnncctcg	ntcatcctct	ctttttcnct	accnccnntt	ctttgcctct	ccttngatca	780

tccaacntc gntggccntn ccccccnnn tcctttncce

820

<210> 27

<211> 818

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(818)

<223> n = A,T,C or G

<400> 27

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tgtttcttct	ccgagcccca	ggcagcgggtg	attcagccct	gcccacactg	attctgatga	120
ctgcgggatgc	tgtgacggac	ccaaggggca	aatagggtcc	caggggtccag	ggagggggcgc	180
ctgctgagca	cttccgcccc	tcacctgcc	cagccccctgc	catgagctct	gggctgggtc	240
tcgcctccca	gggtttctgct	cttccangca	ngccancaag	tggcgtggg	ccacactggc	300
ttcttctctg	cccctccctg	gctctgante	tctgtcttcc	tgctctgtgc	angcnccttg	360
gatctcagtt	tcctcncctc	anngaactct	gtttctgann	tcttcantta	actntgantt	420
tatnacnna	tggnetgtnc	tgtcnnactt	taatgggcn	gaccggctaa	tcctccctc	480
netcccttcc	anttcnnna	accngcttnc	cntctctcc	ccntancccg	ccngggaanc	540
ctcctttgcc	ctnaccang	gccnnnaccg	ccctnnctn	ggggggcnng	gtnnctnenc	600
ctgntnnccc	cncctcncnt	tncctctgcc	cnnncnccgc	nngcannttc	nengtcccn	660
tnnctcttcn	ngntctgnaa	ngntcncntn	tnnnnngn	ngntnntn	tcctctcnc	720
cnnntgnang	tnnttnnnnc	ncngnncccc	nnnnnnnnn	nggnntnnn	tctnncngc	780
cccncccc	ngnatgaag	cctccnntct	ccggccnc			818

<210> 28

<211> 731

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(731)

<223> n = A,T,C or G

<400> 28

aggaagggcg	gagggatatt	gtangggatt	gagggatagg	agnataangg	gggaggtgtg	60
tccaacatg	anggtgnngt	tctcttttga	angaggggtg	ngtttttann	ccnggtgggt	120
gattnaaccc	cattgtatgg	agnnaaaggn	tttnagggat	tttccggctc	ttatcagtat	180
ntanattcct	gtnaatcgga	aaatnatntt	tcnnccggaa	aatnttgctc	ccatccgnaa	240
attnctcccg	ggtagtgcac	nttngggggg	cngccangtt	tcccaggctg	ctanaatcgt	300
actaaagntt	naagtgggan	tncaaataaa	aacctnnac	agagnatecn	taccgcactg	360
tnntttncct	tcgccctntg	actctgcnn	agcccaatac	ccnngnngnat	gtcncnngn	420
nnngcgnenc	tgaaannnnc	tcgnggctnn	gancatcang	gggtttcgca	tcaaaagcnn	480
cgtttcncat	naaggcactt	tngcctcatc	caaccnctng	ccctcnncca	tttngccgtc	540
nggttcncct	acgctnntng	cncctnnntn	ganattttnc	ccgcctnggg	naancctcct	600
gnaatgggta	gggncttntc	ttttnacnnc	nggggtntact	aatcnnctnc	acgctnctt	660
tctenacccc	cccccttttt	caatcccanc	ggcnaatggg	gtctccccnn	cgangggggg	720
nnnccccann	c					731

<210> 29

<211> 822

<212> DNA

<213> Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(822)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 29

actagtccag	tgtgggtggaa	ttccattgtg	ttggggncnc	ttctatgant	antnttagat	60
cgctcanacc	tcacancctc	ccnacnangc	ctataangaa	nannaataga	nctgtncnnt	120
atntntacnc	tcatanncct	cnnacccac	tccctcttaa	ccentactgt	gcctatngcn	180
tnnctantct	ntgccgcctn	cnanccaccn	gtgggcnac	cncnngnatt	ctcnatctcc	240
tcnccatntn	gcctananta	ngtncatacc	ctataacctac	nccaatgcta	nnnctaancn	300
tccatnantt	annntaacta	ccactgaent	ngactttcnc	atnanctcct	aatttgaatc	360
tactctgact	cccacngcct	annnattagc	ancntcccc	nacnatntct	caaccaaadc	420
ntcaacaacc	tatctanctg	ttcnccaacc	nttnctccg	atccccnnac	aacccccctc	480
ccaaataccc	nccacctgac	ncctaaccen	caccatcccg	gcaagccnan	ggncatttan	540
ccactggaat	cacnatngga	naaaaaaaaa	ccnaactctc	tancncnnat	ctcccctaana	600
aatnctcctn	naatttactn	ncantnccat	caancccaen	tgaaacnnaa	ccccctgtttt	660
tanatccctt	ctttcgaaaa	ccnacccttt	annncccaac	ctttngggcc	ccccnctnc	720
ccnaatgaag	gncncccaat	cnangaaacg	ncnttgaaaa	ancnaggcna	anannntccg	780
canatcctat	cccttanttn	ggggncctt	nccnggggcc	cc		822

&lt;210&gt; 30

&lt;211&gt; 787

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(787)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 30

cgggccgctg	ctctggcaca	tgccctctga	atggcatcaa	aagtgatgga	ctgcccattg	60
ctagagaaga	ccttctctcc	tactgtcatt	atggagccct	gcagactgag	ggctcccctt	120
gtctgcagga	tttgatgtct	gaagtctgtg	agtgtggctt	ggagctcctc	atctacatna	180
gctggaagcc	ctggagggcc	tctctcgcca	gcctccccct	tctctccacg	ctctccangg	240
acaccagggg	ctccaggcag	cccattattc	ccagnangac	atggtgtttc	tccacgcgga	300
cccatggggc	ctgnaaggcc	agggctctct	ttgacaccat	ctctcccgtc	ctgectggca	360
ggccgtggga	tcactantt	ctanaacggg	cgccaccncc	gtgggagctc	cagcttttgt	420
tcccnttaat	gaaggttaat	tgcnccgttg	gcgtaatcat	nggtcanaac	tntttcctgt	480
gtgaaattgt	ttntccccct	ncnatccnc	ncnacatacn	aacccgggan	cataaagtgt	540
taaagcctgg	gggtngcctn	nngaataaac	tnaactcaat	taattgcgtt	ggctcatggc	600
ccgctttccn	ttcnggaaaa	ctgtctntcc	ctgcnttntt	gaatcgccca	ccccccnggg	660
aaaagcgggt	tgcnttttng	ggggntcctt	ccncttcccc	cctcnctaan	ccctnccgct	720
cggctcgttc	nggtngcggg	gaanggnat	nnnctccncc	naagggggng	agnnnngntat	780
ccccaaa						787

&lt;210&gt; 31

&lt;211&gt; 799

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(799)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 31

tttttttttt	tttttttggc	gatgctactg	tttaattgca	ggaggtgggg	gtgtgtgtac	60
catgtaccag	ggctattaga	agcaagaagg	aaggaggag	ggcagagcgc	cctgctgagc	120
aacaaaggac	tcctgcagcc	ttctctgtct	gtctcttggc	gcaggcacat	ggggaggcct	180
cccgcagggg	ggggggccacc	agtccagggg	tgggagcact	acanggggtg	ggagtgggtg	240
gtggctggtn	cnaatggcct	gncacanatc	cctacgattc	ttgacacctg	gatttcacca	300
ggggaccttc	tgttctccca	nggnaacttc	ntnnatctcn	aaagaacaca	actgtttctt	360
cngcanttct	ggctgttcat	ggaaagcaca	ggtgtccnat	ttnggctggg	acttgggtaca	420
tatggttccg	gcccacctct	ccntcnaaa	aagtaattca	ccccccccc	ccntctnttg	480
cctgggccc	taantaccca	caccggaact	canttantta	ttcatcttng	gntgggcttg	540
ntnatcnccn	cctgaangcg	ccaagttgaa	aggccacgcc	gtncnccnctc	cccatagnan	600
nttttntnt	canctaatgc	ccccccnggc	aacnatccaa	tcccccccn	tgggggcccc	660
agcccanggc	ccccgntctg	ggnnnccngn	cnegnantcc	ccaggnctctc	ccantcngnc	720
ccnnngcncc	cccgcacgca	gaacanaagg	ntngagccnc	cgcannnnnn	nggtnnncnac	780
ctcgcccccc	ccnnccgng					799

&lt;210&gt; 32

&lt;211&gt; 789

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(789)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 32

tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	60
tttttncnag	ggcaggttta	ttgacaacct	cncgggacac	aancaggctg	gggacaggac	120
ggcaacaggc	tccggcgggc	gcggcgggcg	ccctacctgc	ggtaccaa	ntgcagcctc	180
cgctcccgtc	tgatnttcc	ctgcagctgc	aggatgccnt	aaaacagggc	ctcgcccntn	240
ggtggggacc	ctgggatttn	aatttccacg	ggcacaatgc	ggtcgcancc	cctcaccacc	300
nattaggaat	agtggtnnta	ccnccnccg	ttggencact	ccccttgga	accacttntc	360
gcggctccgg	catctggtct	taaaccttgc	aaacnctggg	gccctctttt	tggttantnt	420
nccngccaca	atcatnactc	agactggcnc	gggctggccc	caaaaaancn	ccccaaaacc	480
ggncatgtc	ttnnccgggt	tgtgtcnatn	tncatcacct	cccgggcnca	ncaggncaac	540
ccaaaagtgc	ttgngggccn	caaaaaanct	ccggggggnc	ccagtttcaa	caaagtcac	600
ccccctggcc	cccaaactct	ccccccgntt	netgggtttg	ggaaccacag	cctctnnctt	660
tggnnngcaa	gntggntccc	ccttcgggce	cccgttgggc	ccnctctaa	ngaaaacncc	720
ntctnnnca	ccatcccccc	nngnnacgnc	tancaangna	tccctttttt	tanaaacggg	780
ccccccnccg						789

&lt;210&gt; 33

&lt;211&gt; 793

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(793)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 33

gacagaacat	gttggatggt	ggagcacctt	tctatacgac	ttacaggaca	gcagatgggg	60
aattcatggc	tgttggagca	atanaacccc	agttctacga	gctgctgac	aaaggacttg	120
gactaaagtc	tgatgaactt	cccaatcaga	tgagcatgga	tgattggcca	gaaatgaana	180
agaagtttgc	agatgtat	gcaaagaaga	cgaaggcaga	gtggtgtcaa	atctttgacg	240
gcacagatgc	ctgtgtgact	ccggttctga	cttttgagga	ggtgttcat	catgatcaca	300
acaangaacg	gggtcgtttt	atcaccantg	aggagcagga	cgtgagcccc	cgcctgcac	360



```

ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc 420
ggncgccacc gcggtggagc tccagctttt gtccctttta gtgagggtta attgcgcgct 480
tggcgtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac 540
acaacatacg anccggaagc atnaaatttt aaagcctggn ggtngcctaa tgantgaact 600
nactcacatt aattggcttt gcgctcactg cccgctttcc agtccggaaa acctgtcctt 660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg 720
cgcncctccc gctttctcgc ttctgaant ccttcccccc ggtctttcgg cttgcggcna 780
acggtatcna cct 793

```

&lt;210&gt; 34

&lt;211&gt; 756

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (756)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 34

```

gcgcgcaccg gcatgtacga gcaactcaag ggcgagtggg accgtaaaag ccccaatctt 60
ancaagtgcg gggaanagct gggtcgactc aagctagttc ttctggagct caacttcttg 120
ccaaccacag ggaccaagct gaccaaagcag cagctaattc tggcccgtag catactggag 180
atcggggccc aatggagcat cctacgcaan gacatccctt ccttcgagcg ctacatggcc 240
cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac 300
cagctcttgg gcctcaacct cctcttcctg ctgtcccaga accgggtggc tgantnccac 360
acgganttgg ancggctgcc tgcccaanga catacanacc aatgtctaca tcnaccacca 420
gtgtectgga gcaatactga tgganggcag ctaccncaaa gtnttcttgg ccnagggtaa 480
catccccgcg cgagagctac accttcttca ttgacatcct gctcgacact atcagggatg 540
aaaatcgcn ggttgctcca gaaaggctnc aanaanatcc ttttcnctga agggccccgg 600
atncnctagt nctagaatcg gcccgccatc gcggtgganc ctccaacctt tcgtnccct 660
ttactgaggg ttnattgccg cccttggcgt tatcatggtc acnccngttn cctgtgttga 720
aattnttaac cccccacaat tccacgcena cattng 756

```

&lt;210&gt; 35

&lt;211&gt; 834

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (834)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 35

```

gggatctctt anactnacct gnatgcatgg ttgtcggtgt ggtcgctgtc gatgaanatg 60
aacaggatct tgcccttgaa gctctcggtt gctgtnttta agttgctcag tctgccgtca 120
tagtcagaca cnetcttggg caaaaaacan caggatntga gtcttgattt cacctccaat 180
aatcttcnng gctgtctgct cgggtgaact gatgacnang ggcagctggt tgtgtntgat 240
aaantccanc angttctcct tggtagacct cccttcaaag ttgttcgggc cttcatcaaa 300
cttctnnaan angannancc canctttgtc gagctggnat ttgganaaca cgtcactgtt 360
ggaaactgat cccaaatggt atgtcatcca tcgctctgct tgccctgaaa aaacttgctt 420
ggcncaaate cgactcccn tccttgaaag aagccnatca cccccctc cctggactcc 480
nncaangact ctncgcctnc cccntccnng cagggttggg ggcannccgg gccntgcgc 540
ttcttcagcc agttcacnat ntcatcagc cctctgcca gctgtntat tccttggggg 600
ggaanccgtc tctcccttcc tgaannaact ttgaccgtng gaatagccgc gcntcnccnt 660
acntnctggg ccgggttcaa antccctcn ttgncnntcn cctcgggcca ttctggattt 720
nccnaacttt tctctcccc cncccnccgg ngtttggntt tttcatnggg ccccaactct 780

```

gctnttggcc antcccctgg gggcntntan cccccctnt ggtcccntng ggcc 834

<210> 36  
 <211> 814  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(814)  
 <223> n = A,T,C or G

<400> 36  
 cggncgcttt ccngccgcgc cccgtttcca tgacnaaggc tcccttcang ttaaatacnn 60  
 cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgcccc 120  
 naacgccaac tcaggccatt cctaccaaag gaagaaaggc tggctctctc accccctgta 180  
 ggaaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgttttact 240  
 aatggaaaaa aaaaataaac aanagggttt gttctcatgg ctgcccaccg cagcctggca 300  
 ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgctctt ttggacatca 360  
 ggcttgatgg tatcaactgcc acntttccac ccagctgggc ncccttcccc catntttgtc 420  
 antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc 480  
 aggggangtc ntttncagtg gatctgccaa anantaccn tatcatcnnt gaataaaaag 540  
 gccctgaac ganatgcttc cancancctt taagacccat aatcctngaa ccatggtgcc 600  
 cttccggtct gatecnaaag gaatgttctt ggggtccant cctcctcttg ttncctacgt 660  
 tgtnttggac cntgtctngn atnacccaan tganatcccc ngaagcacc tncctctggc 720  
 atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcncnnaan 780  
 ggngaactca agaaggtctn ngaaaaacca cncn 814

<210> 37  
 <211> 760  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(760)  
 <223> n = A,T,C or G

<400> 37  
 gcatgtgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg 60  
 gcgcagtgtt cgctgaagg gttgtagtac cagcgcgga tgctctcctt gcagagtcct 120  
 gtgtctggca ggtccacgca atgcccttg tcaactggga aatggatgag ctggagctcg 180  
 tcnaanccac tcgtgtattt ttacangca gcctcctccg aagcntccgg gcagttgggg 240  
 gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt 300  
 gggctgacag gtgccagaac acactggatn ggcctttcca tggaaaggcc tgggggaaat 360  
 cncctnancc caaactgcct ctcaaaggcc accttgacac ccccgacagg ctagaaatgc 420  
 actcttcttc ccaaaggtag ttgttcttgt tgcccaagca ncctccanca aaccaaaanc 480  
 ttgcaaaatc tgctccgtgg gggatcnnn taccanggtt ggggaaanaa acccgcnngn 540  
 gancncctt gtttgaatgc naaggnaata atcctcctgt cttgcttggg tggaanagca 600  
 caattgaact gttaacnttg ggccngttc cncnnggtg gtctgaaact aatcaccgtc 660  
 actggaaaaa ggtangtgcc ttccttgaat tcccaaannt cccctngntt tgggtntttt 720  
 ctcctctncc ctaaaaatcg tnttcccccc cntanggcg 760

<210> 38  
 <211> 724  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(724)  
 <223> n = A,T,C or G

<400> 38  
 tttttttttt tttttttttt tttttttttt ttttttaaaa ccccttccat tgaatgaaaa 60  
 cttccnaaat tgtccaaccc cctcnnccaa atnnccattt ccgggggggg gttccaaacc 120  
 caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa 180  
 aatttaaccc attatnaact taaatncctn gaaacccttg gnttccaaaa atttttaacc 240  
 cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaagggt 300  
 ngatttaaac ccccttnant tnttttnacc cnnngctnaa ntatttngnt tccggtgttt 360  
 tctntntaan cntnggtaac tcccgntaat gaannncctt aanccaatta aaccgaattt 420  
 tttttgaatt ggaaattccn ngggaattna ccgggggttt tcccttttgg gggccatncc 480  
 cccnctttcg ggggttgggn ntaggttgaa tttttnnang nccccaaaaa ncccccaana 540  
 aaaaaactcc caagnnttaa ttngaattnc ccccttccca ggccttttgg gaaaggnggg 600  
 tttntggggg ccngggantt cnttcccccn ttncncccc cccccnggt aaanggttat 660  
 ngnttttggg ttttgggccc cttnanggac cttccggatn gaaattaaat ccccggnccg 720  
 gccg 724

<210> 39  
 <211> 751  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(751)  
 <223> n = A,T,C or G

<400> 39  
 tttttttttt tttttctttg ctcacattta atttttattt tgattttttt taatgctgca 60  
 caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt 120  
 tttattttatt tttactgaaa gtgagaggga acttttgttg ccttttttcc tttttctgta 180  
 ggccgcctta agcttttctaa atttggaaca tctaagcaag ctgaanggaa aagggggttt 240  
 cgcaaatca ctcgggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300  
 ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc ttttaattana 360  
 cttggggggt ccttccccan accaaccctn ctgacaaaaa gtgccngccc tcaaatnatg 420  
 tcccgcnnt cnttgaaaca caengcngaa ngttctcatt ntccccncnc caggtnaaaa 480  
 tgaagggtta ccatntttaa cncacctcc acntggcnnn gcctgaatcc tcnaaaancn 540  
 cctcaancn aattnctnng ccccggtcnc gcntnngtcc cnccggggt ccggaantn 600  
 cccccnga anncnntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc 660  
 cnnagactnt cctcnnncan cncaatttcc ttttnntcac gaacncgnnc cnnaaatgn 720  
 nnnncnctc cnetngtccn naatcnccan c 751

<210> 40  
 <211> 753  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(753)  
 <223> n = A,T,C or G

<400> 40  
 gtgggtatttt ctgtaagatc aggtgttcct cctcgtagg tttagaggaa acaccctcat 60  
 agatgaaaac ccccccgaga cagcagcact gcaactgcc aagcagccgg gtaggagggg 120

cgccctatgc	acagctgggc	ccttgagaca	gcagggcttc	gatgtcaggc	tcgatgtcaa	180
tggctctggaa	gcggcggtg	tacctgcgt	ggggcacacc	gtcagggccc	accaggaact	240
tctcaaagtt	ccaggcaacn	tcgttgcgac	acaccggaga	ccaggtgatn	agcttggggt	300
cggtcataa	cgcggtggcg	tcgtcgttg	gagctggcag	ggcctcccgc	aggaaggcna	360
ataaaaggtg	cgcccccgca	ccgttcanc	cgcacttctc	naanaccatg	angttgggct	420
cnaaccacc	accannccg	acttccttga	nggaattccc	aaatctcttc	gntcttgggc	480
ttctnctgat	gccctanctg	gttgcccngn	atgccaanca	nccccaancc	ccgggggtcct	540
aaanaccn	cctcctcntt	tcctctgggt	tntntcccc	ggaccttggt	tcctctcaag	600
ggancccata	tctcnaccan	tactcacnt	nccccccnt	gnnaccanc	cttctanngn	660
ttcccncccg	ncctctggcc	cntcaaan	gcttnacna	cctgggtctg	ccttcccccc	720
tnccctatct	gnacccn	ttgtctcan	tnt			753

<210> 41  
 <211> 341  
 <212> DNA  
 <213> Homo sapien

<400> 41						
actatatcca	tcacaacaga	catgcttcat	cccatagact	tcttgacata	gcttcaaagt	60
agtgaaccca	tccttgattt	atatacatat	atgttctcag	tattttggga	gcctttccac	120
ttctttaaac	cttggtcatt	atgaacactg	aaaataggaa	tttgtgaaga	gttaaaaagt	180
tatagcttgt	ttacgtagta	agtttttgaa	gtctacattc	aatccagaca	cttagttgag	240
tgtaaaactg	tgatttttaa	aaaatatcat	ttgagaatat	tctttcagag	gtattttcat	300
ttttactttt	tgattaattg	tgttttatat	attagggtag	t		341

<210> 42  
 <211> 101  
 <212> DNA  
 <213> Homo sapien

<400> 42						
acttactgaa	tttagttctg	tgctcttctt	tatttagtgt	tgtatcataa	atactttgat	60
gtttcaaaca	ttctaaataa	ataattttca	gtggcttcat	a		101

<210> 43  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 43						
acatctttgt	tacagtctaa	gatgtgttct	taaatcacca	ttccttctctg	gtcctcaccc	60
tccaggggtg	tctcacactg	taattagagc	tattgaggag	tctttacagc	aaattaagat	120
tcagatgcct	tgctaagtct	agagttctag	agttatgttt	cagaaagtct	aagaaaccca	180
cctcttga	ggtcagtaaa	gaggacttaa	tatttcatat	ctacaaaatg	accacaggat	240
tgatacaga	acgagagtta	tcttgataa	ctcagagctg	agtacctgcc	cgggggccgc	300
tcgaa						305

<210> 44  
 <211> 852  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (852)  
 <223> n = A,T,C or G

<400> 44

acataaatat	cagagaaaag	tagtccttga	aatatttacg	tccaggagtt	ctttgtttct	60
gattatattg	tgtgtgtttt	ggtttgtgtc	caaagtattg	gcagcttcag	ttttcatttt	120
ctctccatcc	tcgggcattc	ttcccaaatt	tatataccag	tcttcgtcca	tccacacgct	180
ccagaatttc	tctttttag	taatatctca	tagctcggct	gagcttttca	taggtcatgc	240
tgctgttggt	cttcttttta	ccccatagct	gagccactgc	ctctgatttc	aagaacctga	300
agacgccctc	agatcgggtc	tcccatttta	ttaatectgg	gttcttgtct	gggttcaaga	360
ggatgtcgcg	gatgaattcc	cataagttag	tccctctcgg	gttgtgtctt	ttggtgtggc	420
acttggcagg	ggggtcttgc	tcctttttca	tatcaggtga	ctctgcaaca	ggaaggtgac	480
tgggtggtgt	catggagatc	tgagcccggc	agaaagtttt	gctgtccaac	aaatctactg	540
tgctaccata	gttgggtgtc	tataaatagt	tctngtcttt	ccagggtgtc	atgatggaag	600
gctcagtttg	ttcagtcttg	acaatgacat	tgtgtgtgga	ctggaacagg	tcactactgc	660
actggccggt	ccacttcaga	tgctgcaagt	tgctgtagag	gagntgcccc	gccgtccctg	720
ccgcccgggt	gaactcctgc	aaactcatgc	tgcaaagggt	ctcgccgttg	atgtcgaact	780
cntggaaagg	gatacaattg	gcattccagct	ggttgggtgtc	caggagggtga	tggagccact	840
cccacacctg	gt					852

<210> 45  
 <211> 234  
 <212> DNA  
 <213> Homo sapien

<400> 45	
acaacagacc	cttgctcgct aacgacctca tgctcatcaa gttggacgaa tccgtgtccg 60
agtctgacac	catccggagc atcagcattg cttcgcagtg ccctaccgcg gggaaactctt 120
gcctcgtttc	tggtctgggt ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg 180
tgaacgtgtc	gggtgtgtct gaggagggtc gcagtaagct ctatgacccg ctgt 234

<210> 46  
 <211> 590  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (590)  
 <223> n = A,T,C or G

<400> 46	
actttttatt	taaatgttta taaggcagat ctatgagaat gatagaaaac atgggtgtgta 60
atttgatagc	aatatttttg agattacaga gtttttagtaa ttaccaatta cacagttaaa 120
aagaagataa	tatattccaa gcanatacaa aatatctaata gaaagatcaa ggcaggaaaa 180
tgantataac	taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta 240
aaagctttta	aaanaanaaa ttattgcagt ctanttaatt caaacagtgt taaatgggtat 300
caggataaan	aactgaaggg canaaagaat taattttcac ttcatgtaac ncacccanat 360
ttacaatggc	ttaaattgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc 420
tggctctctaa	tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag 480
ggctcctgtt	atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct 540
gccttccttt	gaggagactt catctcactg gccaacactc agtcacatgt 590

<210> 47  
 <211> 774  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (774)  
 <223> n = A,T,C or G

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<400> 47
acaagggggc ataatgaagg agtggggana gatttttaaag aaggaaaaaa aacgaggccc      60
tgaacagaat tttcctgnac aacggggctt caaaataatt ttcttgggga ggttcaagac      120
gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg      180
cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaagg ctaatcccaa      240
aacatcaaag aaaggaaggt ggcgtcatat cctccagcct acacagttct ccagggtctct      300
cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctgtgtgt      360
ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgtgat cctgctggc      420
ccacactcct tgaacacaca tccccagggt atattcctgg acatggctga acctcctatt      480
cctacttccg agatgccttg ctccctgcag cctgtcaaaa tccactcac cctccaaacc      540
acggcatggg aagcctttct gacttgctg attactccag catcttgga caatccctga      600
ttccccactc cttagaggca agatagggtg gtttaagagta gggctggacc acttgagacc      660
aggctgctgg cttcaaattt tggctcattt acgagctatg ggaccttggg caagtnatct      720
tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt          774

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<210> 48
<211> 124
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(124)
<223> n = A,T,C or G

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```

<400> 48
canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt      60
ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact      120
tggt                                          124

```

```

<210> 49
<211> 147
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(147)
<223> n = A,T,C or G

```

```

<400> 49
gccgatgcta ctattttatt gcaggagggt ggggtgtttt tattattctc tcaacagctt      60
tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt      120
ttagggcacc catatcccaa gcantgt          147

```

```

<210> 50
<211> 107
<212> DNA
<213> Homo sapien

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```

<400> 50
acattaaatt aataaaagga ctggttgggt tctgctaaaa cacatggctt gatataattgc      60
atggtttgag gttaggagga gttaggcata tgttttggga gaggggt          107

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```

<210> 51
<211> 204
<212> DNA

```

<213> Homo sapien

<400> 51

gtcctaggaa gtctagggga cacacgactc tgggggtcacg gggccgacac acttgacagg	60
cgggaaggaa aggcagagaa gtgacaccgt caggggggaaa tgacagaaag gaaaatcaag	120
gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttgcca	180
cctccctttt gggaccagca atgt	204

<210> 52

<211> 491

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(491)

<223> n = A,T,C or G

<400> 52

acaagataa catttatctt ataacaaaaa ttgatagtt ttaaaggta gtattgtgta	60
gggtattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca	120
ccatcagaca ggttttttaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa	180
aaaacttctt gtatcaattt cttttgttca aaatgactga cttaantatt tttaaatatt	240
tcanaaacac ttcttcaaaa attttcaana tggtagcttt canatgtgcc ctcagtccca	300
atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc	360
atgcaacagt gtcttttctt tnccttttct tttttttttt ttacaggcac agaaactcat	420
caattttatt tggataacaa agggctctca aattatattg aaaaataaat ccaagttaat	480
atcactcttg t	491

<210> 53

<211> 484

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(484)

<223> n = A,T,C or G

<400> 53

acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga	60
gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac	120
actacagaac ccttaaggac actgaaaatt agtaagttaa gttcagaaac attagctgct	180
caatcaaate tctacataac actatagtaa ttaaaacgtt aaaaaaaagt gttgaaatct	240
gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc	300
agctttgant ttctttgtgc tgatangagg aaaggctgaa ttaccttggt gcctctccct	360
aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncc	420
tancttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc	480
cant	484

<210> 54

<211> 151

<212> DNA

<213> Homo sapien

<400> 54

actaaacctc gtgcttgga actccataca gaaaacgggtg ccatccctga acacggctgg	60
ccactgggta tactgctgac aaccgcaaca acaaaaacac aaatccttgg cactggctag	120

tctatgtcct ctcaagtgcc tttttgtttg t 151

<210> 55  
<211> 91  
<212> DNA  
<213> Homo sapien

<400> 55  
acctggett g tctccgggtg gttcccggcg cccccacgg tccccagaac ggacactttc 60  
gccctccagt ggatactga gccaaagtgg t 91

<210> 56  
<211> 133  
<212> DNA  
<213> Homo sapien

<400> 56  
ggcggatgtg cggttggtat atacaaatat gtcattttat gtaagggact tgagtatact 60  
tggatttttg gtatctgtgg gttgggggga cggtcagga accaataccc catggatacc 120  
aagggacaac tgt 133

<210> 57  
<211> 147  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(147)  
<223> n = A,T,C or G

<400> 57  
actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc 60  
gactgggagc tgagcccttc cttttgcgcc tgcctcagag gattgttgcc gacntgcana 120  
tctcantggg ctggatncat gcagggt 147

<210> 58  
<211> 198  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(198)  
<223> n = A,T,C or G

<400> 58  
acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc 60  
tgattacata catttatcct ttaaaaaaga tgtaaactctt aatttttatg ccactctatta 120  
atttaccat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt 180  
ttgacttcta agtttggt 198

<210> 59  
<211> 330  
<212> DNA  
<213> Homo sapien

<400> 59



acaacaaatg ggttgtgagg aagtcttatac agcaaaactg gtgatggcta ctgaaaagat	60
ccattgaaaa ttatcattaa tgattttaaa tgacaagtta tcaaaaactc actcaatttt	120
cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa	180
tacagtcaat aaatgacaaa gccagggcct acaggtgggt tccagacttt ccagacccag	240
cagaaggaat ctattttatac acatggatct ccgtctgtgc tcaaaatacc taatgatatt	300
tttcgtcttt attggacttc tttgaagagt	330

<210> 60  
 <211> 175  
 <212> DNA  
 <213> Homo sapien

<400> 60	
accgtgggtg ccttctacat tcttgacggc tccttcacca acatctgggt ctacttcggc	60
gtcgtgggtc ccttctctct catcctcacc cagctgggtg tgctcatcga ctttgccgac	120
tcctggaacc agcgggtggct gggcaaggcc gaggagtgcg attcccgtgc ctggt	175

<210> 61  
 <211> 154  
 <212> DNA  
 <213> Homo sapien

<400> 61	
accccacttt tcttctgtg agcagtctgg acttctcact gctacatgat gagggtgagt	60
ggttgttgct ctccaacagt atcctccccct ttccggatct gctgagccgg acagcagtgc	120
tggactgcac agccccgggg ctccacattg ctgt	154

<210> 62  
 <211> 30  
 <212> DNA  
 <213> Homo sapien

<400> 62	
cgctcagacc ctatagttag tcgtattaga	30

<210> 63  
 <211> 89  
 <212> DNA  
 <213> Homo sapien

<400> 63	
acaagtcatt tcagcaccct ttgctcttca aaactgacca tcttttatat ttaatgcttc	60
ctgtatgaat aaaaatgggt atgtcaagt	89

<210> 64  
 <211> 97  
 <212> DNA  
 <213> Homo sapien

<400> 64	
accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa gggtctgcag	60
aatcagtgc tccaggattg gtccttggat ctgggggt	97

<210> 65  
 <211> 377  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(377)  
 <223> n = A,T,C or G

<400> 65  
 acaacaanaa ntcccttctt taggccactg atggaaacct ggaaccccct tttgatggca 60  
 gcatggcgctc ctaggccttg acacagcggc tgggggtttgg gctntcccaa accgcacacc 120  
 ccaaccctgg tctacccaca nttctggcta tgggctgtct ctgccactga acatcagggt 180  
 tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa 240  
 ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaaccg 300  
 tgggggtgaa ctaccccccag gaggaatcat gcctggggcga tgcaanggtg ccaacaggag 360  
 gggcgggagg agcatgt 377

<210> 66  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 66  
 acgcctttcc ctcagaattc agggaagaga ctgtcgctg ccttcctccg ttgttgctg 60  
 agaaccctg tggcccttcc caccatatac accctcgctc catctttgaa ctcaaacacg 120  
 aggaactaac tgcaccctgg tcctctcccc agtccccagt tcaccctcca tccctcacct 180  
 tcctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt 240  
 ttatatattt tttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac 300  
 tgttt 305

<210> 67  
 <211> 385  
 <212> DNA  
 <213> Homo sapien

<400> 67  
 actacacaca ctccacttgc ccttggtgaga cactttgtcc cagcacttta ggaatgctga 60  
 ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggc ctgagagttc 120  
 ccctttttaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc 180  
 tgtgctgtgc tggagattca cttttgagag agttctcctc tgagacctga tcttttagagg 240  
 ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300  
 cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgcccatac 360  
 catagtttct gtgctagtgg accgt 385

<210> 68  
 <211> 73  
 <212> DNA  
 <213> Homo sapien

<400> 68  
 acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa 60  
 gtttttttaa tgg 73

<210> 69  
 <211> 536  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(536)

<223> n = A,T,C or G

<400> 69

actagtcag	tgtggtggaa	ttccattgtg	ttgggggctc	tcacctcct	ctcctgcagc	60
tccagctttg	tgctctgcct	ctgaggagac	catggcccag	catctgagta	ccctgctgct	120
cctgctggcc	accctagctg	tggccctggc	ctggagcccc	aaggaggagg	ataggataat	180
ccggggtggc	atctataacg	cagacctcaa	tgatgagtgg	gtacagcgtg	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctgcgggg	300
actaagagcc	aggcaacaga	ccgttggggg	gggtgaattac	ttcttcgacg	tagagggtggg	360
ccgaaccata	tgtaccaagt	cccagcccaa	cttggacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaaacagt	tgtgctcttt	cgagatctac	gaagttccct	ggggagaaca	480
gaangtcctt	gggtgaaatc	caggtgtcaa	gaaatcctan	ggatctgttg	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgacccta	acagggggcc	tctcagccct	cctaattgacc	tccggcctag	ccatgtgatt	60
tcacttccac	tccataacgc	tcctcatact	aggcctacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggc	cttcgatacg	ggataatcct	atttattacc	tcagaagttt	ttttcttcgc	240
agggatTTTT	ctgagccttt	taccactcca	gcctagcccc	taccccccaa	ctaggagggc	300
actggccccc	aacaggcatc	accccgttaa	atcccctaga	agtcccactc	ctaaacacat	360
ccgtattact	cgcatcagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctattttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(533)

<223> n = A,T,C or G

<400> 71

agagctatag	gtacagtgtg	atctcagctt	tgcaaacaca	ttttctacat	agatagtact	60
aggtattaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gattgggtta	120
tgtgatttta	gtggatTTTT	tggcaccctt	atatatgttt	tccaaacttt	cagcagtgat	180
attattttcca	taacttaaaa	agtgagtttg	aaaaagaaaa	tctccagcaa	gcatctcatt	240
taaataaagg	tttgtcatct	ttaaaaatac	agcaatatgt	gactttttta	aaaagctgtc	300
aaataggtgt	gaccctacta	ataattatta	gaaatacatt	taaaaacatc	gagtacctca	360
agtcagtttg	ccttgaaaaa	tatcaaatat	aactcttaga	gaaatgtaca	taaaagaatg	420
cttcgtaatt	ttggagtang	aggttccctc	ctcaattttg	tattttttaaa	aagtacatgg	480
taaaaaaaaa	aattcacaac	agtatataag	gctgtaaaaat	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(511)

<223> n = A,T,C or G

&lt;400&gt; 72

tattacggaa	aaacacacca	cataattcaa	ctancaaaga	anactgcttc	agggcgtgta	60
aaatgaaagg	cttccaggca	gttatctgat	taaagaacac	taaaagaggg	acaaggctaa	120
aagccgcagg	atgtctacac	tatanaggc	gctatctggg	ttggctggag	gagctgtgga	180
aaacatggan	agattggtgc	tgganatcgc	cgtggctatt	cctcattggt	attacanagt	240
gaggttctct	gtgtgcccac	tggtttgaaa	accgttctnc	aataatgata	gaatagtaca	300
cacatgagaa	ctgaaatggc	ccaaaccag	aaagaaagcc	caactagatc	ctcagaanac	360
gcttctaggg	acaataaccg	atgaagaaaa	gatggcctcc	ttgtgcccc	gtctgttatg	420
atttctctcc	attgcagcna	naaacccgtt	cttctaagca	aacncagggtg	atgatggcna	480
aaatacacc	cctcttgaag	naccnggagg	a			511

&lt;210&gt; 73

&lt;211&gt; 499

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(499)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 73

cagtgccagc	actggtgcc	gtaccagtac	caataacagt	gccagtgcc	gtgccagcac	60
cagtgggtggc	ttcagtgtg	gtgccagcct	gaccgccact	ctcacatttg	ggctcttcgc	120
tggccttggt	ggagctgggt	ccagcaccag	tggcagctct	gggtgcctgtg	gtttctccta	180
caagtggat	tttagatatt	gttaatcctg	ccagtctttc	tcttcaagcc	aggggtgcac	240
ctcagaaacc	tactcaacac	agcactctag	gcagccacta	tcaatcaatt	gaagttgaca	300
ctctgcatta	aatctatttg	ccatttctga	aaaaaaaaa	aaaaaaagg	cggccgctcg	360
antctagagg	gcccgtttaa	acccgctgat	cagcctcgac	tgtgccttct	anttgccagc	420
catctgttgt	ttgccccctc	cccgtgcct	tccttgaccc	tggaaagtgc	cactccact	480
gtcctttcct	aantaaat					499

&lt;210&gt; 74

&lt;211&gt; 537

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(537)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 74

tttcatagga	gaacacactg	aggagatact	tgaagaattt	ggattcagcc	gcgaagagat	60
ttatcagctt	aactcagata	aaatcattga	aagtaataag	gtaaaagcta	gtctctaact	120
tccaggccca	cggtcaagt	gaatttgaat	actgcattta	cagtgtagag	taacacataa	180
cattgtatgc	atggaaacat	ggaggaacag	tattacagtg	tcctaccact	ctaatacaaga	240
aaagaattac	agactctgat	tctacagtga	tgattgaatt	ctaaaaatgg	taatcattag	300
ggcttttgat	ttataanact	ttgggtactt	atactaaatt	atggtagtta	tactgccttc	360
cagtttgctt	gatataattg	ttgatattaa	gattcttgac	ttatattttg	aatgggttct	420
actgaaaaan	gaatgatata	ttcttgaaga	catcgatata	catttattta	cactcttgat	480
tctacaatgt	agaaaatgaa	ggaaatgccc	caaattgtat	ggtgataaaa	gtccccgt	537

&lt;210&gt; 75

&lt;211&gt; 467

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(467)  
 <223> n = A,T,C or G

<400> 75  
 caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc 60  
 tgcataattac acgtacctcc tcctgctcct caagtagtgt ggtctatttt gccatcatca 120  
 cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180  
 tggcacaagg aggccatctt ttctcatcgc gttattgtcc ctagaagcgt cttctgagga 240  
 tctagtggg ctttctttct gggtttgggc catttcantt ctcatgtgtg tactattcta 300  
 tcattattgt ataacgggtt tcaaaccngt gggcacncag agaacctcac tctgtaataa 360  
 caatgaggaa tagccacggt gatctccagc accaaatctc tccatgttnt tccagagctc 420  
 ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tcctgn 467

<210> 76  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(400)  
 <223> n = A,T,C or G

<400> 76  
 aagctgacag cattcgggcc gagatgtctc gctccgtggc cttagctgtg ctgcgctac 60  
 tctctctttc tggcctggag gctatccagc gtactccaaa gattcagggt tactcacgtc 120  
 atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg ttcatccat 180  
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagt gagcattcag 240  
 acttgtcttt cagcaaggac tggctctttc atctcttgta ctacactgaa ttcaccccca 300  
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360  
 ttnagtggga tcganacatg taagcagcan catgggaggt 400

<210> 77  
 <211> 248  
 <212> DNA  
 <213> Homo sapien

<400> 77  
 ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60  
 ccagctgcc cggcggggga tgcgaggctc ggagcacctc tgcccggctg tgattgtgtc 120  
 caggcactgt tcatctcagc ttttctgtcc ctttgtctcc ggcaagcgt tctgtgaaa 180  
 gttcatatct ggagcctgat gtcttaacga ataaaggctc catgctccac ccgaaaaaaa 240  
 aaaaaaaa 248

<210> 78  
 <211> 201  
 <212> DNA  
 <213> Homo sapien

<400> 78  
 actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca 60  
 tcacccagac cccgccctgc ccgtgcccc cgtgctgct aacgacagta tgatgcttac 120  
 tctgtactc ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataaatgcct 180  
 gattttaaaaa aaaaaaaaaa a 201

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<210> 79  
 <211> 552  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(552)  
 <223> n = A,T,C or G

<400> 79  
 tccttttgggt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg 60  
 ttttaggcagt gctagtaatt tcctcgtaaat gattctgtta ttactttcct attctttatt 120  
 cctcttttctt ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag 180  
 tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt 240  
 atgcaagtta gtaattactc aggggttaact aaattacttt aatatgctgt tgaacctact 300  
 ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga 360  
 taatattcta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaaattta 420  
 ttcccaggaa tatgggggtc atttatgaat antaccggg anagaagttt tgantnaaac 480  
 cngttttgggt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa 540  
 aaaaaaaaaa aa 552

<210> 80  
 <211> 476  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(476)  
 <223> n = A,T,C or G

<400> 80  
 acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga 60  
 ggggaaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct 120  
 cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt 180  
 gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtacta 240  
 aggttaaaact ttcccacca gaaaaggcaa ctagataaaa atcttagagt actttcatac 300  
 tcttctaagt cctcttcag cctcactttg agtcctcctt gggggttgat aggaantntc 360  
 tcttggttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gcntaaaaat 420  
 gctgaaaaaa ttaaaatgtt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa 476

<210> 81  
 <211> 232  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(232)  
 <223> n = A,T,C or G

<400> 81  
 tttttttttg tatgcentcn ctgtgnggtt attgttgctg ccaccctgga ggagcccagt 60  
 ttcttctgta tctttctttt ctggggggtc ttctggctc tgcccctcca ttcccagcct 120  
 ctcatcccca tcttgactt ttgctagggt tggaggcgt ttcttggtag ccctcagag 180  
 actcagtcag cgggaataag tcctagggtt ggggggtgtg gcaagccggc ct 232

```
<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G
```

<400> 82				60		
aggcgggagc	agaagctaaa	gccaaagccc	aagaagagtg	gcagtgccag	cactgggtgcc	120
agtaccagta	ccaataacat	gccagtgcca	gtgccagcac	cagtggtggc	ttcagtgctg	180
gtgccagcct	gaccgccact	ctcacatttg	ggctcttcgc	tggccttggg	ggagctgggtg	240
ccagcaccag	tggcagctct	ggtgccctgtg	gtttctccta	caagtgagat	tttagatatt	300
gttaatcctg	ccagtccttc	tcttcaagcc	aggggtgcatc	ctcagaaacc	tactcaacac	360
agcactctng	gcagccacta	tcaatcaatt	gaagttgaca	ctctgcatta	aatctatttg	383
ccatttcaaa	aaaaaaaaaa	aaa				

```
<210> 83
<211> 494
<212> DNA
<213> Homo sapien
```

```
<220>  
<221> misc_feature  
<222> (1)...(494)  
<223> n = A,T,C or G
```

<223> H = 107				60		
<400> 83				120		
accgaattgg	gaccgctggc	ttataagcga	tcatgtcctc	cagtattacc	tcaacgagca	180
gggagatcga	gtctatacgc	tgaagaaatt	tgacccgatg	ggacaacaga	cctgtctcagc	240
ccatcctgct	cggttctccc	cagatgacaa	atactctcga	caccgaatca	ccatcaagaa	300
acgcttcaag	gtgctcatga	cccagcaacc	gcgccctgtc	ctctgagggg	ccttaaactg	360
atgtcttttc	tgccactctg	taccctctcg	agactccgta	accaaactct	tcggactgtg	420
agccctgatg	cccttttggc	agccatactc	tttggcntcc	agtctctcgt	ggcgattgat	480
tatgcttgtg	tgaggcaatc	atgggtggcat	caccatnaa	gggaacacat	ttganttttt	540
tttncatat	tttaaattac	naccagaata	nttcagaata	aatgaattga	aaaactctta	600
aaaaaaaaaa	aaaa					660

<210> 84  
<211> 380  
<212> DNA  
<213> Homo sapien

```
<220>  
<221> misc_feature  
<222> (1)...(380)  
<223> n = A,T,C or G
```

<223> H = 174				60	
<400> 84				120	
gctggtagcc	tatggcgtgg	ccacggangg	gctcctgagg	cacgggacag	tgacttccca
agtatcctgc	gccgcgtctt	ctaccgtccc	tacctgcaga	tcttcgggca	gattccccag
gaggacatgg	acgtggccct	catggagcac	agcaactgct	cgctggagcc	cggcttctgg
gcacaccctc	ctggggccca	ggcgggcacc	tgctctccc	agtatgccaa	ctggctgggtg
gtgctgctcc	tctcatctt	cctgctcgtg	gccaacatcc	tgctgggtcac	ttgctcattg
ccatgttcag	ttacacattc	ggcaaagtac	agggcaacag	cnatctctac	tgggaaggcc
agcgttnccg	cctcatccgg				360
					380

<210> 85  
 <211> 481  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(481)  
 <223> n = A,T,C or G

<400> 85  
 gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60  
 tnccatcgctc atactgtagg ttggccacca cctcctgcat cttggggcgg ctaatatcca 120  
 ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180  
 tgtgaaagga tctccagaag gagtgtctga tcttccccac acttttgatg actttattga 240  
 gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtga gtcaccagcc 300  
 ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360  
 ccagattctg cattaccaga nagecgtggc aaaaganatt gacaactcgc ccaggngaa 420  
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<210> 86  
 <211> 472  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(472)  
 <223> n = A,T,C or G

<400> 86  
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 taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180  
 ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240  
 cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt 300  
 catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttggggagctg 360  
 atatntgagc ggaagantag cctttctact tcaccagaca caactccttt catattggga 420  
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<210> 87  
 <211> 413  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(413)  
 <223> n = A,T,C or G

<400> 87  
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 cctcttttgg atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180  
 ttgtcttctg tgtaaatggg actagagaaa acacctatnt tatgagtcaa tctagttngt 240  
 tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg 300



ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aattncataa 360  
acagaaattg ggtngtatat tgaaanann gcatcattnaa acgttttttt ttt 413

<210> 88  
<211> 448  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(448)  
<223> n = A,T,C or G

<400> 88  
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cgtggccctg gccgtgagcc ccgcggccgg ctccagtcce ggcaagccgc cgcgcctggt 180  
gggaggccca tggaccccg cgtggaagaag aagggtgtgcg gcgtgcactg gactttgccc 240  
tcggcnanta caacaaacc gcaacnactt ttaccnagcn cgcgctgcag gttgtgccc 300  
cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng 360  
tttaccagaa ccnagccaat tngaacaatt nccccctcat aacagccctt tttaaaaagg 420  
gaancantcc tgncttttc caaat ttt 448

<210> 89  
<211> 463  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(463)  
<223> n = A,T,C or G

<400> 89  
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agaggtctag gtcctcatat cagcagacag tttgtccgtg tattttgtag ccttgaagtt 180  
ctcagtgcac agttntttct gatgcgaagt tctnatcca gtgttttagt cctttgcac 240  
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tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn 360  
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn 420  
aattcnnana anttcagtn tcatacaaca naacngganc ccc 463

<210> 90  
<211> 400  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(400)  
<223> n = A,T,C or G

<400> 90  
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cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaat 120  
tcttcaccag tcacatcttc taggacctt ttggattcag ttagtataag ctcttcact 180  
tcctttgtta agacttcac tggtaaagtc ttaagttttg tagaaaggaa ttaattgct 240

cgttctctaa caatgtcctc tccttgaagt atttggtga acaaccacc tnaagtcct	300
ttgtgcatcc attttaaata tacttaataag ggcattggt cactaggta aattctgcaa	360
gagtcacatg tctgcaaaag ttgcgttagt atatctgcca	400

<210> 91  
 <211> 480  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(480)  
 <223> n = A,T,C or G

<400> 91	
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ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac	120
atgcctcttt gactaccgtg tgccagtgt ggtgattctc acacacctcc nnccgtcttt	180
tgtggaaaaa ctggcacttg nctggaaacta gcaagacatc acttacaat tcacccacga	240
gacacttgaa aggtgtaaca aagcgactct tgcatgtctt tttgtccctc cggcaccagt	300
tgtcaatact aaccgctgg tttgcctcca tcacatttgt gatctgtagc tctggataca	360
tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt	420
ngatcaggtt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa	480

<210> 92  
 <211> 477  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(477)  
 <223> n = A,T,C or G

<400> 92	
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ggtcccgtg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcctt	120
cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggcttgg ggttgacggg	180
taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccagact gtgcgggacc	240
tgacgcgaaa ctctcgcgatg gtcacgagcg ggaagcgaat gangcccagg gccttgccca	300
gaaccttccg cctgttctct ggcgtcacct gcagctgctg ccgctnacac tcggcctcgg	360
accagcggac aaacggcggtt gaacagcgc acctcacgga tgcccantgt gtcgcgtctc	420
aggaacggcn ccagcgtgct caggtcaatg tcggtgaanc ctccgcgggt aatggcg	477

<210> 93  
 <211> 377  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(377)  
 <223> n = A,T,C or G

<400> 93	
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agtccgagca gccccagacc gctgccgccc gaagctaagc ctgcctctgg ccttcccctc	120
gcctcaatg cagaaccant agtgaggagca ctgtgtttag agttaagagt gaacactgtn	180

tgattttact	tggaatttc	ctctgttata	tagcttttcc	caatgcta	ttccaaacaa	240
caacaacaaa	ataacatgtt	tgctgttna	gttgataaaa	agtangtgat	tctgtatnta	300
aagaaaatat	tactgttaca	tatactgctt	gcaanttctg	tatttattgg	tnctctggaa	360
ataaatatat	tattaaa					377

<210> 94  
 <211> 495  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (495)  
 <223> n = A,T,C or G

<400> 94						60
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cgagctgang	cagatttccc	acagtgacct	cagagccctg	ggctatagtc	tctgaccttc	180
ccaaggaaaag	accaccttct	ggggacatgg	gctggagggc	aggacctaga	ggcaccaagg	240
gaaggcccca	ttccggggct	gttccccgag	gaggaaggga	aggggctctg	tgtgcccccc	300
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tgcaagctca	ccaaggtccc	ctctcagtc	cttccctaca	ccctgaacgg	ncactggccc	420
acacccaccc	agancancca	cccgccatgg	ggaatgttct	caaggaatcg	cngggcaacg	480
tggaactctng	tcccnaagg	gggcagaatc	tccaatagan	gganngaacc	cttgctnana	540
aaaaaaaaana	aaaaa					

<210> 95  
 <211> 472  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (472)  
 <223> n = A,T,C or G

<400> 95						60
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cctctggaag	ccttgcgag	agcggacttt	gtaattgttg	gagaataact	gctgaatttt	180
tagctgtttt	gagttgattc	gcaccactgc	accacaactc	aatatgaaaa	ctatttnact	240
tatttattat	cttgtgaaaa	gtatacaatg	aaaattttgt	tcatactgta	tttatcaagt	300
atgatgaaaa	gcaatagata	tatattcttt	tattatgttn	aattatgatt	gccattatta	360
atcggcaaaa	tgtggagtgt	atgttctttt	cacagtaata	tatgcctttt	gtaacttcac	420
ttggttattt	tattgtaaat	gaattacaaa	attcttaatt	taagaaaatg	gtangttata	480
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<210> 96  
 <211> 476  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (476)  
 <223> n = A,T,C or G

<400> 96						60
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attcttcaca gtagatgatg aaagagtcct ccagtgtctt gngcanaatg ttctagntat 240
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tgtgttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct 360
gcagggtactc ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt 420
tacaaagtct atcttcctca nangtctgtn aaggaacaat ttaatcttct agcttt 476

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<210> 97

<211> 479

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(479)

<223> n = A,T,C or G

<400> 97

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aaataatgct gcaaacttaa tgttcttatg caaaatggaa cgctaatagaa acacagctta 120
caatcgcaaa tcaaaactca caagtgtcga tctgttgtag atttagtgta ataagactta 180
gattgtgctc ctteggatat gattgtttct canatcttgg gcaatnttcc ttagtcaaat 240
caggctacta gaattctgtt attggatatn tgagagcatg aaatttttaa naatacactt 300
gtgattatna aattaatcac aaatttcact tatacctgct atcagcagct agaaaaacat 360
ntnnttttta natcaaagta ttttgtgttt ggaantgtnn aaatgaaatc tgaatgtggg 420
ttcnatctta ttttttcccn gacnactant tnttttttta gggngctattc tganccatc 476

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<210> 98

<211> 461

<212> DNA

<213> Homo sapien

<400> 98

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tgctagttcc tgcactctat tgcctactaa atgcagactg gaggggacca aaaaggggca 120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga 180
agtgaattcag ttctctctac ggatgagaga ctggctcaag aatatectca tgcagcttta 240
tgaagccact ctgaacacgc tggttatcta gatgagaaca gagaaataaa gtcagaaaaat 300
ttacctggag aaaagaggct ttggctgggg accatcccat tgaaccttct cttaggact 360
ttaagaaaaa ctaccacatg ttgtgtatcc tgggtccggc cgtttatgaa ctgaccaccc 420
tttgaataaa tcttgacgt cctgaacttg ctcctctgcg a 461

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<210> 99

<211> 171

<212> DNA

<213> Homo sapien

<400> 99

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gtggcgcgc gcaggtgttt cctcgtaacc cagggccccc tcccttcccc aggcgtccct 60
cggcgctct gcgggccgga ggaggagcgg ctggcgggtg gggggagtgt gaccaccct 120
cggtgagaaa agccttctct agcgatctga gaggcgtgcc ttgggggtac c 171

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<210> 100

<211> 269

<212> DNA

<213> Homo sapien

&lt;400&gt; 100

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cgactgcgac	gacggcggcg	gcgacagtcg	caggtgcagc	gcgggcgcct	ggggtcttgc	120
aaggctgagc	tgacgccgca	gaggtcgtgt	cacgtcccac	gaccttgacg	ccgtcgggga	180
cagccggaac	agagcccggt	gaagcgggag	gcctcgggga	gcccccggg	aagggcgggc	240
cgagagatac	gcaggtgcag	gtggccgcc				269

&lt;210&gt; 101

&lt;211&gt; 405

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 101

tttttttttt	ttttggaatc	tactgcgagc	acagcaggtc	agcaacaagt	ttattttgca	60
gctagcaagg	taacagggtg	gggcatgggt	acatgttcag	gtcaacttcc	tttgtcgtgg	120
ttgattgggt	tgtctttatg	ggggcggggg	ggggtagggg	aaacgaagca	aataacatgg	180
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tgaccgtcat	tttcttgaca	tcaatgttat	tagaagtcag	gatatctttt	agagagtcca	300
ctgttctgga	gggagattag	ggtttcttgc	caaatccaac	aaaatccact	gaaaaagttg	360
gatgatcagt	acgaataccg	aggcatattc	tcatatcggg	ggcca		405

&lt;210&gt; 102

&lt;211&gt; 470

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 102

tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	60
ggcacttaat	ccatttttat	ttcaaaatgt	ctacaaattt	aatcccat	tacgggtatt	120
tcaaaatcta	aattattcaa	attagccaaa	tccttaccaa	ataataccca	aaaatcaaaa	180
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ccgcaaaggt	taaagggaac	aacaaattct	tttacaacac	cattataaaa	atcatatctc	360
aaatcttagg	ggaatatata	cttcacacgg	gatcttaact	tttactcact	ttgtttattt	420
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&lt;210&gt; 103

&lt;211&gt; 581

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 103

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taaatggaaa	ctgccttaga	tacataatc	ttaggaatta	gcttaaaatc	tgccataaag	180
gaaaatcttc	tctagctctt	ttgactgtaa	atttttgact	cttgtaaaac	atccaaatc	240
atttttcttg	tctttaaaat	tatctaattc	ttccattttt	tccctattcc	aagtcaattt	300
gcttctctag	cctcatttcc	tagctcttat	ctactattag	taagtggctt	ttttcctaaa	360
agggaaaaaca	ggaagagaaa	tggcacacaa	aacaaacatt	ttatattcat	atttctacct	420
acgttaataa	aatagcattt	tgtgaagcca	gctcaaaaaga	aggcttagat	ccttttatgt	480
ccatttttagt	cactaaacga	tatcaaagtg	ccagaatgca	aaaggtttgt	gaacatttat	540
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&lt;210&gt; 104

&lt;211&gt; 578

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 104

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&lt;210&gt; 105

&lt;211&gt; 538

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 105

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gtcttgaaca	ccaatattaa	tttgaggaaa	atacaccaaa	atacattaag	taaattattt	180
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&lt;210&gt; 106

&lt;211&gt; 473

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 106

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&lt;210&gt; 107

&lt;211&gt; 1621

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 107

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tagagtaaca cataacattg tatgcatgga aacatggagg aacagtatta cagtgtccta 1260
ccactctaata caagaaaaga attacagact ctgattctac agtgatgatt gaattctaaa 1320
aatggttatc attagggctt ttgatttata aaactttggg tacttatact aaattatggt 1380
agttattctg ccttcagtt tgcttgatat atttgttgat attaagattc ttgacttata 1440
ttttgaatgg gttctagtga aaaaggaatg atatatctt gaagacatcg atatacattt 1500
atttacactc ttgattctac aatgtagaaa atgaggaat gccacaaatt gtatggtgat 1560
aaaagtcacg tgaacaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620
a 1621

```

&lt;210&gt; 108

&lt;211&gt; 382

&lt;212&gt; PRT

&lt;213&gt; Homo. sapien

&lt;400&gt; 108

```

Met Ala Leu Gln Gly Ile Ser Val Met Glu Leu Ser Gly Leu Ala Pro
1          5          10          15
Gly Pro Phe Cys Ala Met Val Leu Ala Asp Phe Gly Ala Arg Val Val
20          25          30
Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
35          40          45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50          55          60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65          70          75          80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85          90          95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100         105         110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115         120         125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130         135         140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145         150         155         160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165         170         175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180         185         190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195         200         205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg
210         215         220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe
225         230         235         240
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro
245         250         255

```

Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala  
 260 265 270  
 Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp  
 275 280 285  
 Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val  
 290 295 300  
 His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu  
 305 310 315 320  
 Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala  
 325 330 335  
 Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu  
 340 345 350  
 Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn  
 355 360 365  
 Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu  
 370 375 380

&lt;210&gt; 109

&lt;211&gt; 1524

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 109

```

ggcacgaggg tgcgccaggg cctgagcgga ggccgggggca gcctcgccag cggggggcccc 60
gggcctggcc atgcctcact gagccagcgc ctgcgcctct acctcgccga cagctggaac 120
cagtgcgacc tagtggtctt cactgtcttc ctccctggcg tgggctgccg gctgaccccg 180
ggtttgtacc acctggggcg cactgtcttc tgcactgact tcatggtttt caccgtgctg 240
ctgcttcaca tcttcacggg caacaaacag ctggggccca agatcgatcat cgtgagcaag 300
atgatgaagg acgtgttctt ctctctcttc ttccctggcg tgtggctggt agcctatggc 360
gtggccacgg aggggctcct gaggccacgg gacagtgact tcccaagtat cctgcgccgc 420
gtcttctacc gtccctacct gcagatcttc gggcagattc cccaggagga catggacgtg 480
gccctcatgg agcacagcaa ctgctcgctg gagcccggtt tctgggcaca cctcctggg 540
gccagcgcg gacactgcgt ctcccagtat gccaaactggc tgggtgtgct gctcctcgct 600
atcttctgct tcgtgggcaa catcctgctg gtcaacttgc tcattgccat gttcagttac 660
acattcgcca aagtacaggg caacagcgat ctctactgga aggcgcagcg ttaccgcctc 720
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cgctcctgct tcaggcaatt gtgcaggcga ccccgagacc cccagccgtc ctccccggcc 840
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gagcgtctga agcgcacgtc ccagaagggt gacttggcac tgaacagct gggacacatc 1020
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ggatcaaggg ctggatcccc ggccgttatc catctggagg ctgcagggtc cttggggtaa 1440
cagggaccac agaccctca ccactcacag attcctcaca ctgggggaaat aaagccattt 1500
cagaggaaaa aaaaaaaaaa aaaa 1524
  
```

&lt;210&gt; 110

&lt;211&gt; 3410

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 110

```

gggaaccagc ctgcacgcgc tggctccggg tgacagccgc gcgcctcggc caggatctga 60
gtgatgagac gtgtccccac tgaggtgccc cacagcagca ggtgttgagc atgggctgag 120
  
```



aagctggacc	ggcaccaaaag	ggctggcaga	aatggggcgcc	tggctgattc	ctaggcagtt	180
ggcggcagca	aggaggagag	gccgcagctt	ctggagcaga	gccgagacga	agcagttctg	240
gagtgcctga	acggcccccct	gagccctacc	cgctggcccc	actatgggtcc	agaggctgtg	300
ggtagagccgc	ctgctgcggc	accggaaaagc	ccagctcttg	ctgggtcaacc	tgctaaccctt	360
tggcctggag	gtgtgttttg	ccgcaggcat	cacctatgtg	ccgcctctgc	tgctggaaagt	420
gggggtagag	gagaagttca	tgaccatggt	gctgggcatt	ggtccagtgc	tgggcctggt	480
ctgtgtcccg	ctcctaggct	cagccagtga	ccactggcgt	ggacgctatg	gccgccggcg	540
gcccttcac	tgggcactgt	ccttggggcat	cctgctgagc	ctctttctca	tcccaagggc	600
cggctggcta	gcagggctgc	tgtgcccga	tcccaggccc	ctggagctgg	cactgctcat	660
cctgggcgtg	gggctgctgg	acttctgtgg	ccagggtgtg	ttcactccac	tggaggccct	720
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cttctcacc	tgcgtagcag	ccacactgct	ggtggctgag	gaggcagcgc	tgggccccac	960
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cggtgccaca	tgcctgtccc	acagtgtggc	cgtggtgaca	gcttcagccg	ccctcaccgg	1440
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gggcatctgc	ctggacctcg	ccatcctgga	tagtgcttcc	ctgctgtccc	aggtggcccc	1800
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cccaactttc	ccctaccccc	aactttcccc	accagctcca	caaccctgtt	tggagctact	3060
gcaggaccag	aagcacaag	tgcggtttcc	caagcctttg	tccatctcag	ccccagagt	3120
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tagcgggggt	aatattttat	actgtaagt	agcaatcaga	gtataatgtt	tatgggtgaca	3300
aaattaaagg	ctttctttata	tgtttaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	3360
aaaaaaaaara	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	3410

&lt;210&gt; 111

&lt;211&gt; 1289

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 111

```

agccaggcgt ccctctgcct gccactcag tggcaacacc cgggagctgt tttgtccttt      60
gtggagcctc agcagttccc tctttcagaa ctactgccca agagccctga acaggagcca      120
ccatgcagtg cttcagcttc attaagacca tgatgatcct cttcaatttg ctcacttttc      180
tgtgtggtgc agccctgttg gcagtgggca tctgggtgtc aatcgatggg gcaccccttc      240
tgaagatcct cgggccactg tcgtccagtg ccatgcagtt tgtcaacgtg ggctacttcc      300
tcatcgcagc cggcgttggt gtctttgtct ttggtttcct gggctgctat ggtgctaaga      360
ctgagagcaa gtgtgccctc gtgacgttct tcttcacect cctcctcacc ttcattgctg      420
aggttgagc tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt      480
tgctggtagt gcctgccatc aagaaagatt atggttccca ggaagacttc actcaagtgt      540
ggaacaccac catgaaaggg ctcaagtgtc gtggcttcac caactatacg gattttgagg      600
actcacccta cttcaaagag aacagtgcct tccccccatt ctggtgcaat gacaacgtca      660
ccaacacagc caatgaaacc tgcaccaagc aaaaggctca cgacaaaaaa gttaggggtt      720
gcttcaatca gcttttgtat gacatccgaa ctaatgcagt caccgtgggt ggtgtggcag      780
ctggaattgg gggcctcgag ctggctgccca tgattgtgtc catgtatctg tactgcaatc      840
tacaataagt ccacttctgc ctctgccact actgctgccca catgggaact gtgaagaggc      900
accctggcaa gcagcagtgga ttgggggagg ggacaggatc taacaatgtc acttgggcca      960
gaatggacct gccctttctg ctccagactt ggggctagat agggaccact ccttttagcg     1020
atgcctgact ttccttccat tgggtgggtg atgggtgggg ggcattccag agcctctaag     1080
gtagccagtt ctgttgccca ttccccagc ctattaaacc cttgatatgc cccctaggcc     1140
tagtggtgat cccagtgtct tactggggga tgagagaaag gcattttata gcctgggcat     1200
aagtgaaatc agcagagcct ctgggtggat gtgtagaagg cacttcaaaa tgcataaacc     1260
tgttacaatg ttaaaaaaaaa aaaaaaaaaa                                1289

```

&lt;210&gt; 112

&lt;211&gt; 315

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 112

```

Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln
 1             5             10             15
Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe
 20             25             30
Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala
 35             40             45
Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu
 50             55             60
Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro
 65             70             75             80
Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser
 85             90             95
Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys
100            105            110
Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Leu Val Ile Phe
115            120            125
Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe
130            135            140
Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys
145            150            155            160
Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu
165            170            175
Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln
180            185            190
Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu

```

195	200	205
His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr		
210	215	220
Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp		
225	230	235
Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val		240
	245	250
Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg		255
	260	265
Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly		270
	275	280
Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly		285
	290	295
Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp		300
305	310	315

&lt;210&gt; 113

&lt;211&gt; 553

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 113

Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala		
1	5	10
Gln Leu Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu		15
	20	25
Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val		30
	35	40
Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly		45
	50	55
Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly		60
	65	70
Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile		75
	85	90
Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu		95
	100	105
Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly		110
	115	120
Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu		125
	130	135
Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala		140
	145	150
Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr		155
	165	170
Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu		175
	180	185
Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu		190
	195	200
Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly		205
	210	215
Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His		220
	225	230
Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu		235
	245	250
Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg		255
	260	265
Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe		270
	275	280
		285

Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val  
 290 295 300  
 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly  
 305 310 315 320  
 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu  
 325 330 335  
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg  
 340 345 350  
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala  
 355 360 365  
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu  
 370 375 380  
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala  
 385 390 395 400  
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly  
 405 410 415  
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu  
 420 425 430  
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala  
 435 440 445  
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser  
 450 455 460  
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala  
 465 470 475 480  
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp  
 485 490 495  
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser  
 500 505 510  
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala  
 515 520 525  
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp  
 530 535 540  
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
 545 550

&lt;210&gt; 114

&lt;211&gt; 241

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 114

Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu  
 1 5 10 15  
 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val  
 20 25 30  
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser  
 35 40 45  
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly  
 50 55 60  
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr  
 65 70 75 80  
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile  
 85 90 95  
 Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr  
 100 105 110  
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys  
 115 120 125  
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met

```

      130      135      140
Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
145      150      155      160
Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
      165      170      175
Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala
      180      185      190
His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
      195      200      205
Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
      210      215      220
Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu
225      230      235      240
Gln

```

```

<210> 115
<211> 366
<212> DNA
<213> Homo sapien

```

```

<400> 115
gctctttctc tccctcctc tgaatttaat tctttcaact tgcaatttgc aaggattaca      60
catttcactg tgatgtatat tgtgttgcaa aaaaaaaaaa gtgtctttgt ttaaaattac      120
ttggttttg aatccatctt gctttttccc cattggaact agtcattaac ccattcttga      180
actggttagaa aaacatctga agagctagtc tatcagcatc tgacagggtga attggatggg      240
tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt      300
tctctacatg cataacaaac cctgctccaa tctgtcacat aaaagtctgt gacttgaagt      360
ttagtc

```

```

<210> 116
<211> 282
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(282)
<223> n = A,T,C or G

```

```

<400> 116
acaaagatga accatttcct atattatagc aaaattaaaa tctaccgcta ttctaattatt      60
gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa      120
agactttact attttcatat ttttaagacac atgattttatc ctatttttagt aacctggttc      180
atacggttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt      240
tcaatctnga actatctana tcacagacat ttctattcct tt

```

```

<210> 117
<211> 305
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(305)
<223> n = A,T,C or G

```

```

<400> 117

```

```

acacatgtcg cttcactgcc ttcttagatg cttctgggtca acatanagga acagggacca      60
tatttatcct ccttcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa      120
aataaggcaa aatatatgaa acaacagggtc tcgagatatt ggaaatcagt caatgaagga      180
tactgatccc tgatcactgt cctaattgcag gatgtgggaa acagatgagg tcacctctgt      240
gactgccccg gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat      300
tggggt                                           305

```

```

<210> 118
<211> 71
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(71)
<223> n = A,T,C or G

```

```

<400> 118
accaaggtgt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa      60
aantcctggg t                                           71

```

```

<210> 119
<211> 212
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(212)
<223> n = A,T,C or G

```

```

<400> 119
actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca      60
gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac      120
agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant      180
aatggantca aganactccc aggcctcagc gt                                           212

```

```

<210> 120
<211> 90
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(90)
<223> n = A,T,C or G

```

```

<400> 120
actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggctcttgcc      60
ctccgccggc gcagaacatg ctgggggtggt                                           90

```

```

<210> 121
<211> 218
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```

&lt;222&gt; (1)...(218)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 121

tgtancgtga anacgacaga nagggttgtc aaaaatggag aanccttgaa gtcattttga	60
gaataagatt tgctaaaaga tttggggcta aaacatgggt attgggagac atttctgaag	120
atatncangt aaattangga atgaattcat gggtcttttg ggaattcctt tacgatngcc	180
agcatanact tcatgtgggg atancagcta cccttgta	218

&lt;210&gt; 122

&lt;211&gt; 171

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 122

taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg	60
catttgtagt ctcatggaac aggaagtcgg atgggtggggc atcttcagtg ctgcatgagt	120
caccaccccg gcggggcat ctgtgccaca ggtccctgtt gacagtgcgg t	171

&lt;210&gt; 123

&lt;211&gt; 76

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(76)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 123

tgtagcgtga agacnacaga atgggtgtgtg ctgtgctatc caggaacaca tttattatca	60
ttatcaanta ttgtgt	76

&lt;210&gt; 124

&lt;211&gt; 131

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 124

acctttcccc aaggccaatg tcctgtgtgc taactggccg gctgcaggac agctgcaatt	60
caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg	120
ttaagatttg t	131

&lt;210&gt; 125

&lt;211&gt; 432

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 125

actttatcta ctggctatga aatagatggg ggaaaattgc gttaccaact ataccactgg	60
cttgaaaaag aggtgatagc tcttcagagg acttgtgact tttgtcaga tgctgaagaa	120
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat	180
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg	240
ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc	300
catgggtgggg gtcttgcac tgtaagaatg gaattgattt tgcttttgca agaattctcag	360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaaccctc agtgcctctc	420
ctctttgctt gt	432

<210> 126  
<211> 112  
<212> DNA  
<213> Homo sapien

<400> 126  
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60  
agtaagaatg atatttcccc ccagggatca ccaaataatt ataaaaattt gt 112

<210> 127  
<211> 54  
<212> DNA  
<213> Homo sapien

<400> 127  
accacgaaac cacaacaag atggaagcat caatccactt gccaaagcaca gcag 54

<210> 128  
<211> 323  
<212> DNA  
<213> Homo sapien

<400> 128  
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc 60  
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120  
ttctctctga agtctaggtt acccattttg gggaccatt ataggcaata aacacagttc 180  
ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt 240  
ttcctgcaaa aggtcactc agtccttgc ttgtcagtg gactgggctc cccagggcct 300  
aggctgcctt cttttccatg tcc 323

<210> 129  
<211> 192  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1) ... (192)  
<223> n = A,T,C or G

<400> 129  
acatacatgt gtgtatattt ttaaataatca cttttgtatc actctgactt tttagcatatc 60  
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc 120  
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg 180  
gataaacaaa gt 192

<210> 130  
<211> 362  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1) ... (362)  
<223> n = A,T,C or G

<400> 130  
ccctttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca 60



tataatgacg caacaaaaag gtgctgttta gtcctatggt tcagtttatg cccttgacaa	120
gtttccattg tgttttgccg atcttctggc taatcgtggg atcctccatg ttattagtaa	180
ttctgtattc cattttgtta acgectggta gatgtaacct gctangaggc taactttata	240
cttatttaaa agctcttatt ttgtgggtcat taaaatggca atttatgtgc agcactttat	300
tgcagcagga agcacgtgtg ggttggttgt aaagctcttt gctaattcta aaaagtaatg	360
gg	362

&lt;210&gt; 131

&lt;211&gt; 332

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(332)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 131

ctttttgaaa gatcgtgtcc actcctgtgg acatcttgtt ttaatggagt ttcccatgca	60
gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga	120
gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc	180
ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttggtttatt atccaactaa	240
cttccatctg ttatcactgg agaaaagccca gactccccan gacnggtacg gattgtgggc	300
atanaaggat tgggtgaagc tggcgttgtg gt	332

&lt;210&gt; 132

&lt;211&gt; 322

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(322)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 132

acttttgcca ttttgtatat ataaacaate ttgggacatt ctcttgaaaa ctaggtgtcc	60
agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat	120
ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggacctttg tatctcgggt	180
tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg	240
ggatgcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct agggaagcct	300
gtaacaatct acaattgggc ca	322

&lt;210&gt; 133

&lt;211&gt; 278

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(278)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 133

acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt	60
cttgtttttc ttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta	120
ctatttaaaa aaaatcacia atctttccct ttaagctatg ttnaattcaa actattcctg	180
ctattcctgt ttgtcaaaag aaattatatt ttccaaaata tgtntatttg ttgatgggt	240

cccacgaaac actaataaaa accacagaga ccagcctg 278

<210> 134

<211> 121

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(121)

<223> n = A,T,C or G

<400> 134

gtttanaaaa cttgttttagc tccatagagg aaagaatggt aaacttttga ttttaaaaca 60  
tgattctctg aggttaaact tggttttcaa atgttatttt tacttgtatt ttgcttttgg 120  
t 121

<210> 135

<211> 350

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(350)

<223> n = A,T,C or G

<400> 135

acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc 60  
atancaagtg gtgactgggt aagcgtgcga caaagggtcag ctggcacatt acttgtgtgc 120  
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtagtcca 180  
gggtgcccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgtc 240  
ccacctcaat caagccctgg gccatgctac ctgcaattgg ctgaacaaac gtttgctgag 300  
ttcccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt 350

<210> 136

<211> 399

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(399)

<223> n = A,T,C or G

<400> 136

tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccagggtt 60  
gctgtgattg tatccgaata ntcctcgtga gaaaagataa tgagatgacg tgagcagcct 120  
gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga 180  
cctggcgggc agccagccag ccacagggtg gcttcttcct tttgtggtga caacnccaag 240  
aaaactgcag agggccaggg tcagggtgtna gtgggtangt gaccataaaa caccagggtc 300  
tcccaggaac ccggggcaaag gccatcccca cctacagcca gcatgcccac tggcgtgatg 360  
ggtgcagang gatgaagcag ccagntgttc tgctgtggt 399

<210> 137

<211> 165

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(165)  
 <223> n = A,T,C or G

<400> 137  
 actggtgtgg tngggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt 60  
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120  
 ttggtgtggtc ccactggtgg tcactgtcat tgggtggggtt cctgt 165

<210> 138  
 <211> 338  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(338)  
 <223> n = A,T,C or G

<400> 138  
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60  
 ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa 120  
 tgctgggcag tctcccatgc cttccacagt gaaagggtt gagaaaaatc acatccaatg 180  
 tcatgtgttt ccagccacac caaaagggtgc ttggggtgga gggctggggg catananggt 240  
 cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa 300  
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139  
 <211> 382  
 <212> DNA  
 <213> Homo sapien

<400> 139  
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa 60  
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccga gtgaaggaga 120  
 attcaaacag acctcgatc tcttggtgtg agcctggtcg gctcaccgcc tatcatctgc 180  
 atttgcctta ctcagggtgt accggactct ggccctgat gtctgtagtt tcacaggatg 240  
 ccttatttgt cttctacacc ccacagggcc ccctacttct tcggatgtgt ttttaataat 300  
 gtcagctatg tgcccatcc tccttcatgc cctccctccc tttcctacca ctgctgagtg 360  
 gcctggaaact tgtttaaagt gt 382

<210> 140  
 <211> 200  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(200)  
 <223> n = A,T,C or G

<400> 140  
 accaaaactt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat 60  
 acttttcat taaacncttt tgttaagtgt caggctgcac tttgtccat anaattattg 120  
 ttttcacatt tcaacttcta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt 180  
 atattcagca taaaggagaa 200

<210> 141  
 <211> 335  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(335)  
 <223> n = A,T,C or G

<400> 141  
 actttatttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg 60  
 ggggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc aggggtttgtt 120  
 atgcatgtag agaaccctaaa ctaattttatt aaacaggata gaaacaggct gtctgggtga 180  
 aatgggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg 240  
 tttttctacc agttcagaga tnggttaatg actanttcca atgggggaaaa agcaagatgg 300  
 attcacaac caagtaattt taaacaaaga cactt 335

<210> 142  
 <211> 459  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(459)  
 <223> n = A,T,C or G

<400> 142  
 accaggttta tattgccaca tatatccttt ccaattgagg gctaaacaga cgtgtattta 60  
 ggggtgttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat 120  
 ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca 180  
 cacatggtcc aacaacactc aaataataaa tcaaataatna tcagatgtta aagattggtc 240  
 ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca 300  
 tcaacacctc agtgggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga 360  
 agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct 420  
 cagcangggg gggaggaacc agctcaacct tggcgctant 459

<210> 143  
 <211> 140  
 <212> DNA  
 <213> Homo sapien

<400> 143  
 acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg 60  
 aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag 120  
 accatccgac ttcctgtgt 140

<210> 144  
 <211> 164  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(164)  
 <223> n = A,T,C or G

&lt;400&gt; 144

acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct	60
atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg	120
aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt	164

&lt;210&gt; 145

&lt;211&gt; 303

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(303)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 145

acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa	60
actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcaggctat	120
gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca	180
gtaggggagt ccatccaagt gacagggtcta atcaaaggag gaaatggaac ataagcccag	240
tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgcccgtg tgattaccat	300
caa	303

&lt;210&gt; 146

&lt;211&gt; 327

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(327)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 146

actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac	60
actggcctgg agtgactcat tgctctgggt ggttgagaga gctcctttgc caacaggcct	120
ccaagtcaagg gctgggattt gtttcctttc cacattctag caacaatatg ctggccactt	180
cctgaacagg gaggggtgga ggagccagca tggaacaagc tgccactttc taaagtagcc	240
agacttgccc ctgggcctgt cacacctact gatgacctt tgtgcctgca ggatggaatg	300
taggggtgag ctgtgtgact ctatggt	327

&lt;210&gt; 147

&lt;211&gt; 173

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(173)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 147

acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg	60
actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt	120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt	173

&lt;210&gt; 148

<211> 477  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(477)  
<223> n = A,T,C or G

<400> 148  
acaaccactt tatctcatcg aatttttaac ccaaactcac tcaactgtgcc tttctatcct 60  
atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact 120  
gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg 180  
gtggctcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgtcac 240  
nccancccac ctccaccgacc ccacccctctt acacagctac ctcccttgctc tctaacccca 300  
tagattatnt ccaaattcag tcaattaagt tactattaac actctaccgg acatgtccag 360  
caccactggg aagccttctc cagccaacac acacacacac acacncacac acacacatat 420  
ccaggcacag gctacctcat cttcacaaat acccctttaa ttaccatgct atgggtgg 477

<210> 149  
<211> 207  
<212> DNA  
<213> Homo sapien

<400> 149  
acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac 60  
taacgtatatt tagagagcca aggaagggtt ctgtggggag tgggatgtaa ggtggggcct 120  
gatgataaat aagagtcagc caggtaagtg ggtgggtgtg tatgggcaca gtgaagaaca 180  
tttcaggcag agggaacagc agtgaaa 207

<210> 150  
<211> 111  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(111)  
<223> n = A,T,C or G

<400> 150  
accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg 60  
cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t 111

<210> 151  
<211> 196  
<212> DNA  
<213> Homo sapien

<400> 151  
agcgcgccag gtcattatga acattccaga tacctatcat tactcgatgc tgttgataac 60  
agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat 120  
ggataccaac cggaaaaccc ctatcccgcg cagcccactg tggccccac tgtctacgag 180  
gtgcatccgg ctcagt 196

<210> 152  
<211> 132  
<212> DNA

<213> Homo sapien

<400> 152

acagcacttt	cacatgtaag	aagggagaaa	ttcctaaatg	taggagaaag	ataacagAAC	60
cttcccttt	tcatctagt	gtggaaacct	gatgctttat	gttgacagga	atagaaccag	120
gagggagt	gt					132

<210> 153

<211> 285

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(285)

<223> n = A,T,C or G

<400> 153

acaanacca	nganaggcca	ctggccgtgg	tgtcatggcc	tccaaacatg	aaagtgtcag	60
cttctgctct	tatgtcctca	tctgacaact	ctttaccatt	tttatcctcg	ctcagcagga	120
gcacatcaat	aaagtccaaa	gtcttggact	tggccttggc	ttggaggaag	tcataaacac	180
cctggctagt	gaggggtcgg	cgccgctcct	ggatgacggc	atctgtgaag	tcgtgcacca	240
gtctgcaggc	cctgtggaag	cgccgtccac	acggagtnag	gaatt		285

<210> 154

<211> 333

<212> DNA

<213> Homo sapien

<400> 154

accacagtcc	tggtgggcca	gggcttcatt	accctttctg	tgaaaagcca	tattatcacc	60
accccaaatt	tttccttaaa	tatctttaac	tgaaggggtc	agcctcttga	ctgcaaagac	120
cctaagccgg	ttacacagct	aactcccact	ggccttgatt	tgtgaaattg	ctgctgcctg	180
attggcacag	gagtcgaagg	tggtcagctc	ccctcctccg	tggaacgaga	ctctgatttg	240
agtttcacaa	attctcgggc	cacctcgtca	ttgctcctct	gaaataaaat	ccggagaatg	300
gtcaggcctg	tctcatccat	atggatcttc	cgg			333

<210> 155

<211> 308

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(308)

<223> n = A,T,C or G

<400> 155

actggaaata	ataaaaacca	catcacagt	ttgtgtcaaa	gatcatcagg	gcatggatgg	60
gaaagtgtct	tggaactgt	aaagtgccta	acacatgata	gatgatTTTT	gttataatat	120
ttgaatcacg	gtgcatacaa	actctcctgc	ctgctcctcc	tgggccccag	ccccagcccc	180
atcacagctc	actgctctgt	tcatccaggc	ccagcatgta	gtggctgatt	cttcttggtc	240
gcttttagcc	tccanaagtt	tctctgaagc	caaccaaacc	tctangtgta	aggcatgctg	300
gccctggt						308

<210> 156

<211> 295

<212> DNA

<213> Homo sapien

<400> 156

accttgctcg	gtgcttgga	catattagga	actcaaaata	tgagatgata	acagtgccta	60
ttattgatta	ctgagagAAC	tgtagacat	ttagttgaag	atcttctaca	caggaactga	120
gaataggaga	ttatgtttg	ccctcatatt	ctctcctatc	ctccttgctt	cattctatgt	180
ctaataatatt	ctcaatcaaa	taaggtttagc	ataatcagga	aatcgaccaa	ataccaatat	240
aaaaccagat	gtctatcctt	aagattttca	aatagaaaac	aaattaacag	actat	295

<210> 157

<211> 126

<212> DNA

<213> Homo sapien

<400> 157

acaagtttaa	atagtgtgt	cactgtgcat	gtgctgaaat	gtgaaatcca	ccacatttct	60
gaagagcaaa	acaaattctg	tcattgtaac	tctatcttgg	gtcgtgggta	tatctgtccc	120
cttagt						126

<210> 158

<211> 442

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(442)

<223> n = A,T,C or G

<400> 158

accactgggt	cttggaaca	cccatcctta	atacgatgat	ttttctgtcg	tgtgaaaatg	60
aanccagcag	gctgccccta	gtcagtcctt	ccttccagag	aaaaagagat	ttgagaaagt	120
gcctgggtaa	ttcaccatta	atttccctcc	ccaaactctc	tgagtcttcc	cttaatatatt	180
ctgggtgggtc	tgaccaaagc	aggtcatggt	ttggtgagca	tttgggatcc	cagtgaagta	240
natgtttgta	gccttgcata	cttagccctt	cccacgcaca	aacggagtgg	cagagtgggtg	300
ccaaccctgt	tttccagtc	cacgtagaca	gattcacagt	gcggaattct	ggaagctgga	360
nacagacggg	ctctttgcag	agccgggact	ctgagangga	catgagggcc	tctgcctctg	420
tgttcattct	ctgatgtcct	gt				442

<210> 159

<211> 498

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(498)

<223> n = A,T,C or G

<400> 159

acttccaggt	aacgttggtg	tttccgttga	gcctgaactg	atgggtgacg	ttgtaggttc	60
tccaacaaga	actgaggttg	cagagcgggt	agggaaagag	gctgttccag	ttgcacctgg	120
gctgctgtgg	actgttggtg	attcctcact	acggcccaag	gttggtggaac	tggcanaaag	180
gtgtgtgtgt	gganttgagc	tcggggcggt	gtggtaggtt	gtgggtctct	caacaggggc	240
tgctgtgggtg	ccggggangt	aangtggtgt	gtcacttgag	cttggccagc	tctggaaagt	300
antanattct	tctgaaggc	cagcgcttgt	ggagctggca	ngggtcantg	ttgtgtgtaa	360
cgaaccagt	ctgctgtggg	tgggtgtana	tcctccacaa	agcctgaagt	tatggtgtcn	420
tcaggtaana	atgtgggttc	agtgtccctg	ggcngctgtg	gaaggttgta	nattgtcacc	480



aagggaataa gctgtggt

498

&lt;210&gt; 160

&lt;211&gt; 380

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(380)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 160

acctgcatcc	agcttccctg	ccaaactcac	aaggagacat	caacctctag	acagggaaac	60
agcttcagga	tacttccagg	agacagagcc	accagcagca	aaacaaatat	tcccatgcct	120
ggagcatggc	atagaggaag	ctganaaatg	tggggctctga	ggaagccatt	tgagtctggc	180
cactagacat	ctcatcagcc	acttgtgtga	agagatgccc	catgacccca	gatgcctctc	240
ccacccttac	ctccatctca	cacacttgag	ctttccactc	tgtataattc	taacatcctg	300
gagaaaaatg	gcagtttgac	cgaacctggt	cacaacggta	gaggctgatt	tctaacgaaa	360
cttgtagaat	gaagcctgga					380

&lt;210&gt; 161

&lt;211&gt; 114

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 161

actccacatc	ccctctgagc	aggcggttgt	cgttcaaggt	gtatttggcc	ttgcctgtca	60
cactgtccac	tgccccctta	tccacttggt	gcttaatccc	tcgaaagagc	atgt	114

&lt;210&gt; 162

&lt;211&gt; 177

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 162

actttctgaa	togaatcaaa	tgatacttag	tgtagtttta	atatcctcat	atatatcaaa	60
gttttactac	tctgataatt	ttgtaaacca	ggtaaccaga	acatccagtc	atacagcttt	120
tggtgatata	taacttgga	ataaccagtc	ctggtgatac	ataaaactac	tcactgt	177

&lt;210&gt; 163

&lt;211&gt; 137

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(137)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 163

catttataca	gacaggcgtg	aagacattca	cgacaaaaac	gcgaaattct	atcccgtgac	60
canagaaggc	agctacggct	actcctacat	cctggcgtgg	gtggccttcg	cctgcacctt	120
catcagcggc	atgatgt					137

&lt;210&gt; 164

&lt;211&gt; 469

&lt;212&gt; DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(469)

<223> n = A,T,C or G

<400> 164

cttatcacaa tgaatgttct cctgggcagc gttgtgatct ttgccacctt cgtgacttta	60
tgcaatgcat catgctatct catacctaata gagggagttc caggagattc aaccaggaaa	120
tgcatggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt	180
gagacatgca cttgctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg	240
ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg	300
gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct	360
tctagtaggc acagggtccc caggccaggc ctcattctcc tctggcctct aatagtcatt	420
gattgtgtag ccatgcctat cagtaaaaag atntttgagc aaacacttt	469

<210> 165

<211> 195

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(195)

<223> n = A,T,C or G

<400> 165

acagtttttt atanatatcg acattgccgg cacttgtgtt cagtttcata aagctgggtgg	60
atccgctgtc atccactatt ccttggctag agtaaaaatt attcttatag cccatgtccc	120
tgcaggccgc ccgcccgtag ttctcggtcc agtcgtcttg gcacacaggg tgccaggact	180
tcctctgaga tgagt	195

<210> 166

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 166

acatcttagt agtgtggcac atcagggggc catcagggtc acagtcactc atagcctcgc	60
cgaggtcgga gtccacacca ccggtgtagg tgtgtcfaat cttgggcttg gcgcccacct	120
ttggagaagg gatatgctgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt	180
tttgagacc agcctgagca aggggcggat gttcagcttc agtcctcctc tcgtcagggtg	240
gatgccaaac tcgtctangg tccgtgggaa gctgggtgtcc acntcaccta caacctgggc	300
gangatctta taaagaggct ccnagataaa ctccacgaaa cttctctggg agctgctagt	360
nggggccttt ttggtgaact ttc	383

<210> 167

<211> 247

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(247)  
 <223> n = A,T,C or G

<400> 167

acagagccag accttgGCCa taaatgaanc agagattaag actaaacccc aagtcganat	60
tggagcagaa actggagcaa gaagtgggCC tggggctgaa gtagagacca aggccactgc	120
tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac	180
tcaatctgan tccaaagtgg tggctggaac actggctcatg acanaggcag tgactctgac	240
tgangtc	247

<210> 168  
 <211> 273  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(273)  
 <223> n = A,T,C or G

<400> 168

acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa	60
aatccctcan ccttggttctt cactactgtc tatactgana gtgtcatgtt tccacaaagg	120
gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag taggggtggc	180
aattcccaac ttccttgcca caagcttccc aggtttctc ccctggaaaa ctccagcttg	240
agtcccatgat acatctcatgg gctgccctgg gca	273

<210> 169  
 <211> 431  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(431)  
 <223> n = A,T,C or G

<400> 169

acagccttgg cttcccca aa ctccacagtc tcagtgcaga aagatcatct tccagcagtc	60
agctcagacc aggggtcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta	120
ctactgtcaa atgaccccc atacttcctc aaaggctgtg gtaagttttg cacaggtag	180
ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccacactgac	240
cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcaactgctgg gcaccagctc	300
acgcacatca ctgacaaccg ggatggaaaa agaantgcc aacttcatac atccaactgg	360
aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc	420
tcgaacactg a	431

<210> 170  
 <211> 266  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(266)  
 <223> n = A,T,C or G

&lt;400&gt; 170

acctgtgggc	tgggctgtta	tgcctgtgcc	ggctgctgaa	agggagtcca	gaggtggagc	60
tcaaggagct	ctgcaggcat	tttgccaanc	ctctccanag	canagggagc	aacctacact	120
ccccgctaga	aagacaccag	attggagtcc	tgggaggggg	agttgggggtg	ggcatttgat	180
gtatacttgt	cacctgaatg	aangagccag	agaggaanga	gacgaanatg	anattggcct	240
tcaaagctag	gggtctggca	gggtgga				266

&lt;210&gt; 171

&lt;211&gt; 1248

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1248)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 171

ggcagccaaa	tcataaacgg	cgaggactgc	agcccgcact	cgcagccctg	gcaggcggca	60
ctgggtcatgg	aaaacgaatt	gttctgctcg	ggcgctcctg	tgcattccgca	gtgggtgctg	120
tcagccgcac	actgtttcca	gaagtgagtg	cagagctcct	acaccatcgg	gctgggcctg	180
cacagtcttg	aggccgacca	agagccagg	agccagatgg	tggaggccag	cctctccgta	240
cggcaccag	agtacaacag	acccttgctc	gctaacgacc	tcatgctcat	caagttggac	300
gaatccgtgt	ccgagtctga	caccatccgg	agcatcagca	ttgcttcgca	gtgccctacc	360
gcggggaact	cttgccctcgt	ttctggctgg	ggctgctg	cgaacggcag	aatgcctacc	420
gtgctgcagt	gcgtgaacgt	gtcgggtggg	tctgaggagg	tctgcagtaa	gctctatgac	480
ccgctgtacc	accccagcat	gttctgcgcc	ggcggagggc	aagaccagaa	ggactcctgc	540
aacggtgact	ctggggggcc	cctgatctgc	aacgggtact	tgcagggcct	tgtgtctttc	600
ggaaaagccc	cgtgtggcca	agttggcgtg	ccagggtgtc	acaccaacct	ctgcaaattc	660
actgagtgga	tagagaaaac	cgtccaggcc	agttaactct	ggggactggg	aacctatgaa	720
attgaccccc	aaatacatcc	tgcggaagga	attcaggaat	atctgttccc	agccccctct	780
ccctcaggcc	caggagtcca	ggcccccagc	ccctcctccc	tcaaaccaag	ggtacagatc	840
cccagcccct	cctcccctcag	acccaggagt	ccagaccccc	cagccccctc	tccctcagac	900
ccaggagtcc	agccccctct	ccctcagacc	caggagtcca	gacccccccag	ccccctctcc	960
ctcagaccga	gggggtccagg	cccccaaccc	ctcctccctc	agactcagag	gtccagagccc	1020
ccaaccntc	attccccaga	cccagaggtc	cagggtccag	ccccctntcc	ctcagaccga	1080
gcggtccaat	gccacctaga	ctntccctgt	acacagtgcc	cccttgtggc	acgttgaccc	1140
aaccttacca	gttggttttt	catttttngt	ccctttcccc	tagatccaga	aataaagttt	1200
aagagaagng	caaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa		1248

&lt;210&gt; 172

&lt;211&gt; 159

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(159)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 172

Met	Val	Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Pro
1				5				10					15		
Leu	Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser
			20					25				30			
Glu	Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr
		35					40				45				
Ala	Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly

50		55		60
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu				
65		70		75
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe				80
	85		90	95
Cys Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser				
	100		105	110
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe				
	115		120	125
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn				
	130		135	140
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser				
145	150		155	

&lt;210&gt; 173

&lt;211&gt; 1265

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1265)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 173

ggcagcccg	actcgagcc	ctggcaggcg	gcactgggtca	tggaaaacga	attgttctgc	60
tcgggcggtcc	tggtgcatcc	gcagtgggtg	ctgtcagccg	cacactgttt	ccagaactcc	120
tacaccatcg	ggctgggctt	gcacagtctt	gaggccgacc	aagagccagg	gagccagatg	180
gtggaggcca	gcctctccgt	acggcaccca	gagtacaaca	gaccttgc	cgctaacgac	240
ctcatgctca	tcaagttgga	cgaatccgtg	tccgagtctg	acaccatccg	gagcatcagc	300
attgcttcgc	agtgccctac	cgcggggaac	tcttgccctg	tttctggctg	gggtctgctg	360
gcgaacggtg	agctcacggg	tgtgtgtctg	ccctcttcaa	ggaggtcctc	tgcccagtcg	420
cgggggctga	cccagagctc	tgcgctccag	gcagaatgcc	taccgtgctg	cagtgcgtga	480
acgtgtcggg	gggtgtctgag	gagggtctgca	gtaagctcta	tgaccgctg	taccaccca	540
gcatgttctg	cgccggcgga	gggcaagacc	agaaggactc	ctgcaacggg	gactctgggg	600
ggccctgat	ctgcaacggg	tacttgagg	gccttgtgtc	tttcggaaaa	gccccgtgtg	660
gccaaagtgg	cgtgccagg	gtctacacca	acctctgcaa	attcactgag	tggatagaga	720
aaaccgtcca	ggccagttaa	ctctggggac	tgggaaccca	tgaattgac	ccccaaatac	780
atcctgcgga	aggaattcag	gaatatctgt	tcccagcccc	tcctccctca	ggcccaggag	840
tccaggcccc	cagccctcc	tccctcaaac	caagggtaca	gatccccagc	ccctcctccc	900
tcagacccag	gagtcagac	ccccagccc	ctcctccctc	agacccagga	gtccagcccc	960
tcctccntca	gacccaggag	tccagacccc	ccagccctc	ctccctcaga	cccagggggt	1020
gaggccccca	acccctcctc	cttcagagtc	agagggtccaa	gcccccaacc	cctcgttccc	1080
cagacccaga	ggttnaggtc	ccagccctc	tccntcaga	cccagnnggtc	caatgccacc	1140
tagattttcc	ctgnacacag	tgcccccttg	tggngangttg	acccaacctt	accagttggt	1200
ttttcatatt	tngtcccttt	cccctagatc	cagaaataaa	gtttaagaga	ngngcaaaaa	1260
aaaaa						1265

&lt;210&gt; 174

&lt;211&gt; 1459

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1459)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 174

ggtcagccgc	acactgtttc	cagaagtgag	tgcagagctc	ctacaccatc	gggctggggc	60
tgcacagtct	tgaggccgac	caagagccag	ggagccagat	ggtggaggcc	agcctctccg	120
tacggcacc	agagtacaac	agacccttgc	tgcctaacga	cctcatgctc	atcaagttag	180
acgaatccgt	gtccgagttc	gacaccatcc	ggagcatcag	cattgcttcg	cagtgcctta	240
ccgcggggaa	ctcttgcttc	gtttctggct	gggtctgct	ggcgaacggt	gagctcacgg	300
gtgtgtgtct	gccctcttca	aggaggtcct	ctgcccagtc	gcgggggctg	acccagagct	360
ctgcgtccca	ggcagaatgc	ctaccgtgct	gcagtgcgtg	aacgtgtcgg	tggtgtctga	420
ngagggtctgc	antaagctct	atgacccgct	gtaccacccc	ancatgttct	gcgccggcgg	480
agggcaagac	cagaaggact	cctgcaacgt	gagagagggg	aaaggggagg	gcaggcgact	540
caggggaaggg	tggagaaggg	ggagacagag	acacacaggg	ccgcatggcg	agatgcagag	600
atggagagag	acacagggag	acagtgacaa	ctagagagag	aaactgagag	aaacagagaa	660
ataaacacag	gaataaagag	aagcaaaagg	agagagaaac	agaaacagac	atggggaggc	720
agaaacacac	acacatagaa	atgcagttga	ccttccaaca	gcattggggc	tgagggcggt	780
gacctccacc	caatagaaaa	tcctcttata	acttttgact	ccccaaaaac	ctgactagaa	840
atagcctact	gttgacgggg	agccttacca	ataacataaa	tagtgcattt	atgcatacgt	900
tttatgcatt	catgatatac	ctttgttgga	attttttgat	atttctaagc	tacacagttc	960
gtctgtgaat	ttttttaaat	tggtgcaact	ctcctaaaat	ttttctgatg	tgtttattga	1020
aaaaatccaa	gtataagtgg	acttgtgcat	tcaaaccagg	gttgttcaag	ggtcaactgt	1080
gtaccacag	ggaaacagtg	acacagattc	atagaggtga	aacacgaaga	gaaacaggaa	1140
aatcaagac	tctacaaaga	ggctgggcag	gggtggctcat	gcctgtaatc	ccagcacttt	1200
gggaggcgag	gcaggcgagat	cacttgaggt	aaggagttca	agaccagcct	ggccaaaatg	1260
gtgaaatcct	gtctgtacta	aaaatacaaa	agttagctgg	atatggtggc	aggcgctctg	1320
aatcccagct	acttggggagg	ctgaggcagg	agaattgctt	gaatatggga	ggcagaggtt	1380
gaagtgaagt	gagatcacac	cactatactc	cagctggggc	aacagagtaa	gactctgtct	1440
caaaaaaaaa	aaaaaaaaa					1459

&lt;210&gt; 175

&lt;211&gt; 1167

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1167)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 175

gcgcagccct	ggcaggcggc	actggtcagt	gaaaaacgaat	tgttctgctc	gggcgtcctg	60
gtgcatccgc	agtgggtgct	gtcagccgca	cactgtttcc	agaactccta	caccatcggg	120
ctgggcctgc	acagtcttga	ggccgaccaa	gagccaggga	gccagatggt	ggaggccagc	180
ctctccgtac	ggcaccacga	gtacaacaga	ctcttgctcg	ctaacgacct	catgctcatc	240
aagttggacg	aatccgtgtc	cgagtctgac	accatccgga	gcatacagcat	tgcttcgcag	300
tgccctaccg	cggggaactc	ttgcctcgtn	tctggctggg	gtctgctggc	gaacggcaga	360
atgcctaccg	tgtgtcactg	cgtgaacgtg	tcggtgggtg	ctgaggangt	ctgcagtaag	420
ctctatgacc	cgctgtacca	ccccagcatg	ttctgcgccc	gcggaggggc	agaccagaag	480
gactcctgca	acggtgactc	tggggggccc	ctgatctgca	acgggtactt	gcagggcctt	540
gtgtctttcg	gaaaagcccc	gtgtggccaa	cttggcgtgc	caggtgtcta	caccaacctc	600
tgcaaatcca	ctgagtggat	agagaaaacc	gtccagncca	gttaactctg	gggactggga	660
acccatgaaa	ttgaccccca	aatacatcct	gcggaaangaa	ttcagggaata	tctgttccca	720
gcccctcctc	cctcaggccc	aggagtccag	gccccagccc	cctcctccct	caaaccaagg	780
gtacagatcc	ccagcccttc	ctccctcaga	cccaggagtc	cagacccccc	agccctcnt	840
ccntcagacc	caggagtcca	gcccctcctc	cntcagacgc	aggagtccag	accccccagc	900
ccntcntccg	tcagacccag	gggtgcaggc	ccccaaaccc	tcntccntca	gagtcagagg	960
tccaagcccc	caaccctctg	ttccccagac	ccagaggtnc	aggtcccagc	ccctcctccc	1020
tcagacccag	cgggtccaatg	ccacctagan	tnccctgtta	cacagtgcct	ccttgtggca	1080
ngttgaccca	accttaccag	ttggtttttc	attttttgtc	cctttccctt	agatccagaa	1140
ataaagtnta	agagaagcgc	aaaaaaa				1167

<210> 176  
 <211> 205  
 <212> PRT  
 <213> Homo sapien  
 <220>  
 <221> VARIANT  
 <222> (1)...(205)  
 <223> Xaa = Any Amino Acid

<400> 176  
 Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp  
 1 5 10 15  
 Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu  
 20 25 30  
 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val  
 35 40 45  
 Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu  
 50 55 60  
 Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser  
 65 70 75 80  
 Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly  
 85 90 95  
 Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met  
 100 105 110  
 Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val  
 115 120 125  
 Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala  
 130 135 140  
 Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly  
 145 150 155 160  
 Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys  
 165 170 175  
 Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys  
 180 185 190  
 Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser  
 195 200 205

<210> 177  
 <211> 1119  
 <212> DNA  
 <213> Homo sapien

<400> 177  
 ggcgactcgc agccctggca ggcggcactg gtcattggaaa acgaattggt ctgctcgggc 60  
 gtcttggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctctacacc 120  
 atcgggctgg gctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag 180  
 gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg 240  
 ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct 300  
 tcgcagtgcc ctaccgctgg gaactcttgc ctctgttctg gctggggtct gctggcgaac 360  
 gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc 420  
 caaccctggc aggggtgtac catttcggca acttccagtg caaggacgtc ctgctgcattc 480  
 ctactgggt gctcactact gctcactgca tcaccgggaa cactgtgatc aactagccag 540  
 caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600  
 actaacctat ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660  
 cagttatcct cactgaattg agatttcctg cttcagtgtc agccattccc acataatttc 720  
 tgacctacag aggtgagggg tcatatagct cttcaaggat gctggtactc ccctcacaac 780

```

ttcattttctc ctgttgtagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca      840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg      900
ctcagtacac cagggcaggt ctacgatttc ttcatttagt gtatgctgtc cattcatgca      960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg     1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc     1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaaa     1119

```

&lt;210&gt; 178

&lt;211&gt; 164

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(164)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 178

```

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1           5           10           15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
          20          25          30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
          35          40          45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
          50          55          60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
65          70          75          80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
          85          90          95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
          100         105         110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
          115         120         125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
          130         135         140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
145         150         155         160
Pro Gly Thr Leu

```

&lt;210&gt; 179

&lt;211&gt; 250

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 179

```

ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct      60
ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct     120
gccaggcaact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga     180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa     240
aaaaaaaaaa                                     250

```

&lt;210&gt; 180

&lt;211&gt; 202

&lt;212&gt; DNA

&lt;213&gt; Homo sapien



<400> 180  
 actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca 60  
 tcaccacagac cccgcccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta 120  
 ctctgtctact cggaaactat ttttatgtaa ttaatgtatg ctttcttggt tataaatgcc 180  
 tgatttaaaa aaaaaaaaaa aa 202

<210> 181  
 <211> 558  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(558)  
 <223> n = A,T,C or G

<400> 181  
 tccytttght naggtttkkg agacamccck agacctwaan ctgtgtcaca gacttcyngg 60  
 aatgttttagg cagtgttagt aatttcytcg taatgattct gttattactt tcctnattct 120  
 ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa 180  
 ggtagtgtga tagtataagt atctaagtc agatgaaagt gtgttatata tatccattca 240  
 aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaac 300  
 ctactctgtt ccttggttag aaaaaattat aaacaggact ttgttagttt gggaagccaa 360  
 attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw 420  
 ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt 480  
 aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc 540  
 caaaaaaaaa aaaaaaaaaa 558

<210> 182  
 <211> 479  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(479)  
 <223> n = A,T,C or G

<400> 182  
 acagggwttk grggatgcta agsccccrga rwtygtttga tccaaccctg gcttwttttc 60  
 agaggggaaa atggggccta gaagttacag mscatytagy tggtgcmgtg gcacccttg 120  
 cstcacacag astcccaggt agctgggact acaggcacac agtcactgaa gcaggccctg 180  
 ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240  
 ctaagggtta actttccac ccagaaaagg caacttagat aaaatcttag agtactttca 300  
 tactmttcta agtctcttc cagcctcact kkgagtcctm cytgggggtt gataggaant 360  
 ntctcttggc tttctcaata aartctctat ycatctcatg ttttaatttg tacgcatara 420  
 awtgstgara aaattaaaat gttctggtty macttttaaa aaaaaaaaaa aaaaaaaaaa 479

<210> 183  
 <211> 384  
 <212> DNA  
 <213> Homo sapien

<400> 183  
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc 60  
 agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtgttgg cttcagtgtc 120  
 ggtgccagcc tgaccgccac tctcacattt gggctcttcg ctggccttgg tggagctggt 180  
 gccagcacca gtggcagctc tggtgcctgt gggttctctc acaagtgaga ttttagatat 240

tgtaaatcct gccagtcttt ctcttcaagc caggggtgcat cctcagaaac ctactcaaca	300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt	360
gccatttcaa aaaaaaaaaa aaaa	384

&lt;210&gt; 184

&lt;211&gt; 496

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(496)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 184

accgaattgg gaccgctggc ttataagcga tcatgtyynt ccrgtatcac ctcaacgagc	60
agggagatcg agtctatacg ctgaagaaat ttgacccgat gggacaacag acctgctcag	120
cccattcctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga	180
aacgcttcaa ggtgctcatg acccagcaac cgcgcctgt cctctgaggg tcccttaaac	240
tgatgtcttt tctgccacct gttacccctc ggagactccg taaccaaaact cttcggactg	300
tgagccctga tgcccttttg ccagccatac tctttggcat ccagtctctc gtggcgattg	360
attatgcttg tgtgaggcaa tcatggtggc atcacccata aagggaacac atttgacttt	420
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst	480
taaaaaaaaa aaaaaa	496

&lt;210&gt; 185

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 185

gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtgacttcc	60
caagtatcyt ggcsgcgtc ttctaccgtc cctacctgca gatcttcggg cagattcccc	120
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct	180
gggcacaccc tccctggggc caggcgggca cctgcgtctc ccagtatgcc aactggcttg	240
tggtgctgct cctcgtcatc ttctgctcgt tggccaacat cctgctggtc aactgctca	300
ttgccatgtt cagttacaca ttccggcaaag tacagggcaa cagcgatctc tactgggaag	360
gcgcagcgtt accgcctcat ccgg	384

&lt;210&gt; 186

&lt;211&gt; 577

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(577)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 186

gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggctctctgc ttcataccgc	60
tnccatcgtc atactgtagg tttgccacca cytcttgga tcttggggcg gcntaatatt	120
ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctgggtc tgtcttcgc	180
tcggtgtgaa aggatctccc agaaggagtg ctcgatcttc cccacacttt tgatgacttt	240
attgagtoga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgagggtcac	300
cagccctata atgcggttga mcgtgccgaa garcaccgag ccttgtgtgg gggkkgaagt	360
ctcaccaga ttctgcatta ccagagagcc gtggcaaaag acattgacaa actcgccag	420
gtggaaaaag amcamctcct ggargtgcctn gccgctctc gtcmtgtgtt ggcagcgctw	480

tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcacatcc 540  
aagatntcgc acagcactna tccagttggg attaaat 577

<210> 187  
<211> 534  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(534)  
<223> n = A,T,C or G

<400> 187  
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaaticatw 60  
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact 120  
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtcctggg aakaagggta 180  
tgccctattc acacctgtta aaaggcgct aagcattttt gattcaacat cttttttttt 240  
gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc 300  
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag ctttygggagc 360  
tgatatttga gcggaagagt agccttttcta cttcaccaga cacaactccc tttcatattg 420  
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttctgttctg 480  
aggatctccc agttttattta ccacttgcac aagaaggcgt tttcttcctc aggc 534

<210> 188  
<211> 761  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(761)  
<223> n = A,T,C or G

<400> 188  
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaatth ttgtgtgcgtg 60  
tgtgtgtgcg cgcataattat atagacaggc acatcttttt tacttttgta aaagcttatg 120  
cctcttttgg atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180  
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt 240  
tttattcgac atgaaggaaa ttccagatn acaacactna caaactctcc ctkgackarg 300  
ggggacaaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa 360  
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtktt wttctccctt 420  
gcaaaaaaca tgtacngact tcccgttgag taatgccaaag ttgttttttt tatnataaaa 480  
cttgcccttc attacatgtt tnaaagtggg gtggtgggccc aaaatattga aatgatggaa 540  
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac 600  
atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaatata ctttgaacta 660  
tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac 720  
gaaaataata acattgaaga aaaaananaaa aaanaaaaaa a 761

<210> 189  
<211> 482  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(482)  
<223> n = A,T,C or G

&lt;400&gt; 189

tttttttttt	tttgcgatn	ctactatttt	attgcaggan	gtgggggtgt	atgcaccgca	60
caccggggct	atnagaagca	agaaggaagg	agggagggca	cagccccttg	ctgagcaaca	120
aagccgectg	ctgccttctc	tgtctgtctc	ctgggtgcagg	cacatgggga	gaccttcccc	180
aaggcagggg	ccaccagtcc	aggggtggga	atacaggggg	tgggangtgt	gcataagaag	240
tgataggcac	aggccacccg	gtacagaccc	ctcggctcct	gacaggtnga	tttcgaccag	300
gtcattgtgc	cctgcccagg	cacagcgtan	atctggaaaa	gacagaatgc	tttccttttc	360
aaatttggct	ngtcatngaa	ngggcanttt	tccaanttng	gctnggtcct	ggtacncttg	420
gttcggccca	gctccncgtc	caaaaantat	tcaccnnct	ccnaattgct	tgcnggnccc	480
cc						482

&lt;210&gt; 190

&lt;211&gt; 471

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(471)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 190

tttttttttt	ttttaaaaca	gtttttcaca	acaaaattta	ttagaagaat	agtgggtttt	60
aaaactctcg	catccagtga	gaactaccat	acaccacatt	acagctngga	atgtntctcca	120
aatgtctggg	caaatgatac	aatggaacca	ttcaatctta	cacatgcacg	aaagaacaag	180
cgcttttgac	atacaatgca	caaaaaaaaa	aggggggggg	gaccacatgg	attaaaattt	240
taagtactca	tcacatacat	taagacacag	ttctagtcca	gtcnaaaatc	agaactgcnt	300
tgaaaaattt	catgtatgca	atccaaccaa	agaacttnat	tggtgatcat	gantnctcta	360
ctacatcnac	cttgatcatt	gccaggaacn	aaaagttnaa	ancacncngt	acaaaaanaa	420
tctgtaattn	anttcaacct	ccgtacngaa	aaatnttntt	tatacactcc	c	471

&lt;210&gt; 191

&lt;211&gt; 402

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(402)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 191

gagggattga	aggtctgttc	tastgtcggm	ctgttcagcc	accaactcta	acaagttgct	60
gtcttccact	cactgtctgt	aagcttttta	accagacwg	tatcttcata	aatagaacaa	120
attcttcacc	agtcacatct	tctaggacct	ttttggattc	agttagtata	agctcttcca	180
cttcctttgt	taagacttca	tctggtaaa	tcttaagttt	tgtagaaagg	aattyaattg	240
ctcgttctct	aacaatgtcc	tctccttgaa	gtatttggct	gaacaacca	cctaaagtcc	300
ctttgtgcat	ccatttttaa	tatacttaat	agggcattgk	tnactaggt	taaattctgc	360
aagagtcac	tgtctgcaaa	agttgcgtta	gtatatctgc	ca		402

&lt;210&gt; 192

&lt;211&gt; 601

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(601)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 192

```

gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnnaact    60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac    120
atgcytyttt gaytaccgtg tgccaagtgc tgggtattct yaacacacyt ccatccccgt    180
cttttggtga aaaactggca cttktctgga actagcarga catcacttac aaattcaccc    240
acgagacact tgaagggtgt aacaaagcga ytcttgcat gctttttgtc cctccggcac    300
cagttgtcaa tactaaccgc ctggtttgcc tccatcacat ttgtgatctg tagctctgga    360
tacatctcct gacagtactg aagaacttct tcttttgttt caaaagcarg tcttggtgcc    420
tggtggatca ggttcccatt tcccagtcyg aatgttcaca tggcatattt wacttcccac    480
aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag    540
cctcgatgta gccggccagc gccaaaggcag ggcgcgtgag ccccaccagc agcagaagca    600
g

```

&lt;210&gt; 193

&lt;211&gt; 608

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(608)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 193

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atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact    60
ggtcccgcgt tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt    120
cccaacgcag gcagmagcgg gscgggtcaa tgaactccay tcgtggcttg gggtkgacgg    180
tkaagtgcag gaagaggctg accacctcgc ggtccaccag gatgcccgac tgtgcgggac    240
ctgcagcgaa actcctcgat ggtcatgagc gggaaagcgaa tgaggcccag ggccttgccc    300
agaaccttcc gcctgttctc tggcgtcacc tgcagctgct gccgctgaca ctcggcctcg    360
gaccagcgga caaacggcrt tgaacagccg cacctcacgg atgcccagtg tgtcgcgctc    420
caggammgsc accagcggtt ccagggtcaat gtcggtgaag ccctccgcgg gtrattggcgt    480
ctgcagtggt tttgtcgatg ttctccaggg acaggctggc cagctgcggt tcatcgaaga    540
gtcgcgccctg cgtgagcagc atgaaggcgt tgtcggctcg cagttcttct tcaggaaactc    600
cacgcaat

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&lt;210&gt; 194

&lt;211&gt; 392

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(392)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 194

```

gaacggctgg accttgccct gcattgtgct tgctggcagg gaataccttg gcaagcagyt    60
ccagtcggag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc    120
tccgcctcaa tgcagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg    180
tttgatttta cttgggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac    240
aacaacaaca aaataacatg tttgcctggt aagttgtata aaagtaggtg attctgtatt    300
taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktnctstgg    360
aaataaatat agttattaaa gggtgtcant cc

```

<210> 195  
 <211> 502  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(502)  
 <223> n = A,T,C or G

<400> 195  
 ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg 60  
 ccgagctgag gcagatgttc ccacagtgc cccagagcc stgggstata gtytctgacc 120  
 cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc 180  
 aaggggaaggc ccatttccgg ggstgttccc cgaggaggaa gggaaggggc tctgtgtgcc 240  
 ccccasgagg aagaggccct gagtcctggg atcagacacc ccttcacgtg tatccccaca 300  
 caaatgcaag ctcaaccaagg tccccctcga gtcccccttc stacaccctg amcggccact 360  
 gscscacacc caccagagc acgccacccg ccatggggar tgtgctcaag gartcgcnng 420  
 gcarcgtgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmstt 480  
 gctnanaaaa aaaaanaaaa aa 502

<210> 196  
 <211> 665  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(665)  
 <223> n = A,T,C or G

<400> 196  
 ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60  
 cctctggaag ccttgcgag agcggacttt gtaattgttg gagaataact gctgaatttt 120  
 wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga 180  
 actwatttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkac 240  
 aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt 300  
 attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact 360  
 tcacttggtt attttattgt aaatgartta caaaattcct aatttaagar aatggtatgt 420  
 watatttatt tcattaattt ctttcctkgt ttacgtwaat ttgaaaaga wtgcattgatt 480  
 tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt 540  
 ttcttagaat gtataaagggt tgtagcccat cnaacttcaa agaaaaaaat gaccacatac 600  
 tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan 660  
 aagtg 665

<210> 197  
 <211> 492  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(492)  
 <223> n = A,T,C or G

<400> 197  
 tttntttttt ttttttttgc aggaaggatt ccatttattg tggatgcatt ttcacaatat 60  
 atgtttattg gagcgatcca ttatcagtga aaagatcaaa gtgtttataa natttttagg 120

```

aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtna gatnacagag      180
aattatagtc naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa      240
caaaattcta cctgaaact tactccatcc aaatattgga ataanagtca gcagtgatac      300
attctcttct gaacttttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct      360
tgttcaaaag tacaacnaag caatgttccc ttacatagg ccttaattca aactttgatc      420
catttcactc ccatcacggg agtcaatgct acctgggaca cttgtatttt gttcatnctg      480
ancntggctt aa                                                              492

```

<210> 198

<211> 478

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (478)

<223> n = A,T,C or G

<400> 198

```

tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa      60
tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac      120
tgagtatatt ttgaaaagga caagttaa aa gtanacncat attgccganc atancacatt      180
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaanaaat      240
natatatgtc aatcngattt aagatacaaa acagatccta tggtagatan catcntgtag      300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta      360
agcattctag tacctctact ccatggttaa gaatcgtaca cttatgttta catatgtnc a      420
gggtaagaat tgtgttaagt naanttatgg agagggtccan gagaaaaatt tgaatncaa      478

```

<210> 199

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (482)

<223> n = A,T,C or G

<400> 199

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agtgacttgt cctccaacaa aacccttga tcaagtttgt ggcactgaca atcagaccta      60
tgctagtacc tgtcatctat tcgctactaa atgcagactg gagggggacca aaaaggggca      120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga      180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta      240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga      300
aaatttacct ggangaaaag aggctttngg ctggggacca tccattgaa ccttctctta      360
anggacttta agaanaaaact accacatgtn tgtngtatcc tgggtgccngg ccgtttantg      420
aacntngacn ncacccttnt ggaatanant cttgacngcn tctgaactt gtcctctgc      480
ga                                                              482

```

<210> 200

<211> 270

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (270)

<223> n = A,T,C or G

<400> 200  
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgccca gcagttggtc 60  
cgactgcgac gacggcgggc ggcacagtcg caggtgcagc gcggggcgcc ggggtcttgc 120  
aaggctgagc tgacgccgca gaggtcgtgt cacgtcccac gaccttgacg ccgtcgggga 180  
cagccggaac agagcccggg gaangcggga ggcctcgggg agcccctcgg gaagggcggc 240  
ccgagagata cgcaggtgca ggtggccgcc 270

<210> 201

<211> 419

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(419)

<223> n = A,T,C or G

<400> 201  
tttttttttt ttttggaaatc tactgcgagc acagcaggtc agcaacaagt ttatttttgc 60  
gctagcaagg taacagggtg gggcatgggt acatgttcag gtcaacttcc tttgtcgtgg 120  
ttgattggtt tgtctttatg ggggcggggg ggggtagggg aaancgaagc anaantaaca 180  
tgagtggttg gcacctctcc tgtagaacct ggttacnaaa gcttggggca gttcacctgg 240  
tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatatc ttttagagag 300  
tccactgtnt ctggaggagg attagggttt cttgccaana tccaancaa atccacntga 360  
aaaagtggga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcca 419

<210> 202

<211> 509

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(509)

<223> n = A,T,C or G

<400> 202  
tttntttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60  
tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng 120  
gtnattnnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaatnnaa 180  
tacnncaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa 240  
aatatatacg gctggtggtt tcaaagtaca attatcttaa cactgcaaac atnttttnnaa 300  
ggaactaaaa taataaaaaa cactnccgca aagggttaaag ggaacaacaa attcntttta 360  
caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng 420  
ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca 480  
caatggnaat nccnccnccncc tggactagt 509

<210> 203

<211> 583

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(583)

<223> n = A,T,C or G



&lt;400&gt; 203

tttttttttt	ttttttttga	ccccctctt	ataaaaaaca	agttaccatt	ttattttact	60
tacacatatt	tattttataa	ttggtattag	atattcaaaa	ggcagctttt	aaaatcaaac	120
taaatggaaa	ctgccttaga	tacataattc	ttaggaatta	gcttaaaatc	tgccataaagt	180
gaaaatcttc	tctagctctt	ttgactgtaa	atttttgact	cttgtaaaac	atccaaattc	240
atttttcttg	tctttaaaaa	tatctaattc	ttccattttt	tccctattcc	aagtcaattt	300
gcttctctag	cctcatttcc	tagctcttat	ctactattag	taagtggctt	ttttcctaaa	360
agggaaaaca	ggaagagana	atggcacaca	aaacaaacat	tttatattca	tatttctacc	420
tacgttaata	aaatagcatt	ttgtgaagcc	agctcaaaag	aaggcttaga	tccttttatg	480
tccatttttag	tactaaacg	atattcnaag	tgccagaatg	caaaagggtt	gtgaacattt	540
attcaaaagc	taatataaga	tatttcacat	actcatcttt	ctg		583

&lt;210&gt; 204

&lt;211&gt; 589

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (589)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 204

ttttttttnt	tttttttttt	tttttttctc	ttcttttttt	ttganaatga	ggatcgagtt	60
tttcactctc	tagatagggc	atgaagaaaa	ctcatctttc	cagctttaaa	ataacaatca	120
aatctcttat	gctatatcat	attttaagtt	aaactaatga	gtcactggct	tatcttctcc	180
tgaaggaaat	ctgttcattc	ttctcattca	tatagttata	tcaagtacta	ccttgcatat	240
tgagagggtt	ttcttctcta	tttacacata	tatttccatg	tgaatttgta	tcaaacottt	300
attttcatgc	aaactagaaa	ataatgtntt	cttttgcata	agagaagaga	acaatatnag	360
cattacaaaa	ctgctcaaat	tgtttggtta	gnttatccat	tataattagt	tnnggcaggag	420
ctaatacaaa	tcacattttac	ngacnagcaa	taataaaaact	gaagtaccag	ttaaatatcc	480
aaaataatta	aaggaacatt	tttagcctgg	gtataattag	ctaattcact	ttacaagcat	540
ttattnagaa	tgaattcaca	tgttattatt	ccntagccca	acacaatgg		589

&lt;210&gt; 205

&lt;211&gt; 545

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (545)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 205

tttttntttt	ttttttcagt	aataatcaga	acaatattta	tttttatatt	taaaattcat	60
agaaaagtgc	cttacattta	ataaaagttt	gtttctcaaa	gtgatcagag	gaattagata	120
tngtcttgaa	caccaatatt	aatttgagga	aaatacacca	aaatacatta	agtaaattat	180
ttaagatcat	agagcttgta	agtgaaaaaga	taaaatttga	cctcagaaac	tctgagcatt	240
aaaaatccac	tattagcaaa	taaattacta	tggaacttctt	gctttaattt	tgtgatgaat	300
atgggggtgc	actgggtaac	caacacattc	tgaaggatac	attacttagt	gatagattct	360
tatgtacttt	gctanatnac	gtggatatga	gttgacaagt	ttctctttct	tcaatctttt	420
aaggggcnga	ngaaatgagg	aagaaaagaa	aaggattacg	catactgttc	tttctatngg	480
aaggattaga	tatgtttcct	ttgccaatat	taaaaaaata	ataatgttta	ctactagtga	540
aaccc						545

&lt;210&gt; 206

&lt;211&gt; 487

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(487)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 206

tttttttttt	tttttttagtc	aagttttctna	tttttattat	aattaaagtc	ttggtcattt	60
cattttattag	ctctgcaact	tacatatatta	aattaaagaa	acgttnttag	acaactgtna	120
caattttataa	atgtaagggtg	ccattattga	gtanatatat	tcctccaaga	gtggatgtgt	180
ccctttctccc	accaactaat	gaancagcaa	cattagttta	attttattag	tagatnatac	240
actgctgcaa	acgctaattc	tcttctccat	ccccatgtng	atattgtgta	tatgtgtgag	300
ttggttnagaa	tgcatacanca	atctnacaat	caacagcaag	atgaagctag	gcntgggctt	360
tcgggtgaaaa	tagactgtgt	ctgtctgaat	caaagtatct	gacctatcct	cgggtggcaag	420
aactcttcga	accgcttctc	caaaggcngc	tgccacattt	gtggcntctn	ttgcacttgt	480
ttcaaaa						487

&lt;210&gt; 207

&lt;211&gt; 332

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(332)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 207

tgaattggct	aaaagactgc	atttttanaa	ctagcaactc	ttatttcttt	cctttaaaaa	60
tacatagcat	taaatcccaa	atcctattta	aagacctgac	agcttgagaa	ggtcactact	120
gcatttatag	gaccttctgg	tggttctgct	gttacntttg	aantctgaca	atccttgana	180
atcctttgcat	gcagaggagg	taaaagggtat	tggattttca	cagaggaana	acacagcgca	240
gaaatgaagg	ggccaggctt	actgagcttg	tccactggag	ggctcatggg	tgggacatgg	300
aaaagaaggc	agcctaggcc	ctggggagcc	ca			332

&lt;210&gt; 208

&lt;211&gt; 524

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(524)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 208

agggcggtgg	gcgaggggcg	ttactgtttt	gtctcagtaa	caataaatac	aaaaagactg	60
gttgtgttcc	ggccccatcc	aaccacgaag	ttgattttctc	ttgtgtgcag	agtgactgat	120
tttaaaggac	atggagcttg	tcacaatgtc	acaatgtcac	agtggtgaagg	gcacactcac	180
tcctcgctga	ttcacattta	gcaaccaaca	atagctcatg	agtccatact	tgtaaatact	240
tttggcagaa	tacttnttga	aacttgcaga	tgataactaa	gatccaagat	atttcccaaa	300
gtaaatagaa	gtgggtcata	atattaatta	cctgttcaca	tcagcttcca	tttacaagtc	360
atgagcccag	acactgacat	caaactaagc	ccacttagac	tcctcaccac	cagtctgtcc	420
tgatcatcaga	caggaggctg	tcaccttgac	caaattctca	ccagtcaatc	atctatccaa	480
aaaccattac	ctgatccact	tccggtaatg	caccaccttg	gtga		524

<210> 209  
 <211> 159  
 <212> DNA  
 <213> Homo sapien

<400> 209  
 ggggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg 60  
 tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca 120  
 caaaggactc tcgacccaaa ctgcccaga cctctcca 159

<210> 210  
 <211> 256  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (256)  
 <223> n = A,T,C or G

<400> 210  
 actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc 60  
 actgaatttc tttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta 120  
 tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat 180  
 ttgcaggggtg naaatggan ggctggtttg ttanatgaac agggacatag gaggtaggca 240  
 ccaggatgct aaatca 256

<210> 211  
 <211> 264  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (264)  
 <223> n = A,T,C or G

<400> 211  
 acattgtttt tttgagataa agcattgaga gagctctcct taacgtgaca caatggaagg 60  
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120  
 atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga 180  
 ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga 240  
 aaaaaaggag caaatgagaa gcct 264

<210> 212  
 <211> 328  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (328)  
 <223> n = A,T,C or G

<400> 212  
 acccaaaaat ccaatgctga atatttggtc tcattattcc canattcttt gattgtcaaa 60  
 ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag 120  
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag 180

ttnaatttca	ttccattga	cttgggatcc	ttatcatcag	ccagagagat	tgaaaattta	240
cccctacnac	tctttactct	ctgganaggg	ccagtgggtg	tagctataag	cttggccaca	300
tttttttttc	ctttattcct	ttgtcaga				328

&lt;210&gt; 213

&lt;211&gt; 250

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (250)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 213

acttatgagc	agagcgacat	atccnagtgt	agactgaata	aaactgaatt	ctctccagtt	60
taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaagta	agccaaggct	120
cattatgccca	aagganatat	acattttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatattt	gcatgaacct	gctgataanc	catgttaana	aacaaatata	tctctnacct	240
tctcatcggt						250

&lt;210&gt; 214

&lt;211&gt; 444

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (444)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 214

accagaatc	caatgctgaa	tatttggctt	cattattccc	agattctttg	attgtcaaag	60
gatttaagt	tgtctcagct	tgggcacttc	agttaggacc	taaggatgcc	agccggcagg	120
tttatatatg	cagcaacaat	attcaagcgc	gacaacagg	tattgaaact	gcccggcagg	180
tgaatttcat	tccattgac	ttgggaccc	tatcatcagc	canagagatt	gaaaatttac	240
ccctacgact	ctttactctc	tggagagggc	cagtgggtgg	agctataagc	ttggccacat	300
ttttttttcc	tttattcctt	tgtcagagat	gcgattcatc	catatgctan	aaaccaacag	360
agtgaacttt	acaaaattcc	tataganatt	gtgaataaaa	ccttacctat	agttgccatt	420
actttgctct	ccctaataata	cctc				444

&lt;210&gt; 215

&lt;211&gt; 366

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (366)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 215

acttatgagc	agagcgacat	atccaagtgt	anactgaata	aaactgaatt	ctctccagtt	60
taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaagta	agccaaggct	120
cattatgccca	aagganatat	acattttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatattt	gcatgaacct	gctgataagc	catgttgaga	aacaaatata	tctctgacct	240
tctcatcggt	aagcagaggc	tgtaggcaac	atggaccata	gcgaanaaaa	aacttagtaa	300
tccaagctgt	tttctacact	gtaaccagg	ttccaaccaa	ggtggaaatc	tcctatactt	360

ggtgcc

366

<210> 216  
 <211> 260  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(260)  
 <223> n = A,T,C or G

<400> 216  
 ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc 60  
 caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc atttttttat 120  
 taataaaaag tnnaaaaggc ctcttctcaa cttttttccc ttnggctgga aaatttaaaa 180  
 atcaaaaatt tcctnaagtt ntcaagctat catatatact ntatcctgaa aaagcaacat 240  
 aattcttctt tccctccttt 260

<210> 217  
 <211> 262  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(262)  
 <223> n = A,T,C or G

<400> 217  
 acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta 60  
 tcttgccctat aattttctat ttaataaagg aaatagcaaa ttgggggtggg gggaatgtag 120  
 ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt 180  
 atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta 240  
 atatccttca tgcttgtaaa gt 262

<210> 218  
 <211> 205  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(205)  
 <223> n = A,T,C or G

<400> 218  
 accaaggtgg tgcattaccg gaantggatc aangacacca tctgtggccaa cccctgagca 60  
 cccctatcaa ctcccttttg tagtaaaactt ggaaccttgg aaatgaccag gccaaagactc 120  
 aggcctcccc agttctactg acctttgtcc ttangnttna ngtcagggt tgctaggaaa 180  
 anaaatcagc agacacaggt gtaaa 205

<210> 219  
 <211> 114  
 <212> DNA  
 <213> Homo sapien

<400> 219

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accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220  
<211> 93  
<212> DNA  
<213> Homo sapien

<400> 220  
actagccagc acaaaaggca gggtagcctg aattgcttct tgcctctttac atttctttta 60  
aaataagcat ttagtgctca gtcctactg agt 93

<210> 221  
<211> 167  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(167)  
<223> n = A,T,C or G

<400> 221  
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tcttttgccc agcctgtggc tctactgtag taagtttctg ctgatgagga gccagnatgc 120  
ccccactac cttccctgac gtcctccana aatcacccaa cctctgt 167

<210> 222  
<211> 351  
<212> DNA  
<213> Homo sapien

<400> 222  
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gttcttcacc tgtcccccaa tccttaaaag gccatactgc ataaagtcaa caacagataa 120  
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180  
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240  
taggtgagca tgattagaga gcttgtaggt tgcttttaca tatatctggc atatttgagt 300  
ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t 351

<210> 223  
<211> 383  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(383)  
<223> n = A,T,C or G

<400> 223  
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ttaaaatgtc tgtgccaaaa ttttgatatt tatttgagga cttcttatca aaagtaatgc 180  
tgccaaagga agtctaagga attagtagtg ttcccmteac ttgtttggag tgtgctatcc 240  
taaaagattt tgatttcctg gaatgacaat tatattttta ctttggtggg ggaaanagtt 300  
ataggaccac agtcttccct tctgatactt gtaaattaat cttttattgc acttgttttg 360  
accattaagc tatatgttta aaa 383

<210> 224  
 <211> 320  
 <212> DNA  
 <213> Homo sapien

<400> 224  
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 aaaagtttgt gacattgtag tagggagtgt gtacccctta ctcccatca aaaaaaaat 120  
 ggatacatgg ttaaaggata raagggaat attttatcat atgttctaaa agagaaggaa 180  
 gagaaaatac tactttctcr aaatggaagc ccttaaagggt gctttgatac tgaaggacac 240  
 aaatgtggcc gtccatcctc ctttaragtt gcatgacttg gacacggtaa ctgttgtagt 300  
 tttaractcm gcattgtgac 320

<210> 225  
 <211> 1214  
 <212> DNA  
 <213> Homo sapien

<400> 225  
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 aactcctaca ccatcgggct gggcctgcac agtcttgagg ccgaccaaga gccagggagc 180  
 cagatggttg aggccagcct ctccgtacgg caccagagt acaacagacc ctgtctcgt 240  
 aacgacctca tgctcatcaa gttggacgaa tccgtgtccg agtctgacac catccggagc 300  
 atcagcattg cttcgcagtg cctaccgcg gggaactctt gcctcgtttc tggctgggggt 360  
 ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaacgtgtc ggtggtgtct 420  
 gaggaggtct gcagtaagct ctatgacccg ctgtaccacc ccagcatgtt ctgcgccggc 480  
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 ggtgtctaca ccaacctctg caaattcact gagtggatag agaaaaccgt ccaggccagt 660  
 taactctggg gactgggaac ccatgaaatt gacccccaaa tacatcctgc ggaaggaatt 720  
 cagcaaatatc tgttcccagc cctcctccc tcaggcccag gattccaggc ccccagcccc 780  
 tcctccctca aaccaagggt acagatcccc agccccctct cctcagacc caggagtcca 840  
 gacccccag cccctcctcc ctccagacca ggagtccagc cctcctccc tcagaccag 900  
 gattccagac ccccagccc ctctcctc agaccagggt gtccaggccc ccaaccctc 960  
 ctccctcaga ctccagaggt caagccccc accctcctt cccagaccc agaggtccag 1020  
 gtcccagccc ctctcctc agaccagcg gtccaatgcc acctagactc tccctgtaca 1080  
 cagtgcctcc ttgtggcacg ttgacccaac cttaccagtt ggtttttcat tttttgtccc 1140  
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 aaaaaaaaaa aaaa 1214

<210> 226  
 <211> 119  
 <212> DNA  
 <213> Homo sapien

<400> 226  
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 agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcacg ataaccagt 119

<210> 227  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<400> 227  
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acggacgggtt	cttagcacaa	tttgtgaaat	ctgtgtaraa	cggggctttg	cagggggagat	180
aattttcttc	ctctggagga	aaggtgggtga	ttgacaggca	gggagacagt	gacaaggcta	240
gagaaagcca	cgctcggcct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
gcttgteccc	ttccaatcag	ccacttctga	gaacccccat	ctaacttcct	actggaaaag	360
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gacaggctct	gccctcaagc	cggctgaggg	cagcaaccac	tctcctcccc	tttctcacgc	660
aaagccattc	ccacaaatcc	agaccatacc	atgaagcaac	gagacccaaa	cagtttggct	720
caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
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&lt;210&gt; 228

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 228

actggagaca	ctgttgaact	tgatcaagac	ccagaccacc	ccaggctctcc	ttcgtgggat	60
gtcatgacgt	ttgacatacc	tttggaaagc	gcctcctcct	tgggaagatgg	aagaccgtgt	120
tcgtggccga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
taggaaaagt	ggcttcgtaa	aatagaagag	cagtcaactgt	ggaactacca	aatggcgaga	240
tgctcgggtg	acattggggg	gctttgggat	aaaagattta	tgagccaact	attctctggc	300
accagattct	aggccagttt	gttccactga	agcttttccc	acagcagtc	acctctgcag	360
gctggcagct	gaatggcttg	ccggtggctc	tgtggcaaga	tcacactgag	atcgatgggt	420
gagaaggcta	ggatgcttgt	ctagtgttct	tagctgtcac	gttggctcct	tccaggttgg	480
ccagacggtg	ttggccactc	ccttctaaaa	cacaggcgcc	ctcctggtga	cagtgaccgc	540
ccgtggatg	ccttggccca	ttccagcagt	cccagttatg	catttcaagt	ttgggggttg	600
ttcttttcgt	taatgttcc	ctgtgttgct	agctgtcttc	atttctctgg	ctaagcagca	660
ttgggagatg	tggaccagag	atccactcct	taagaaccag	tggcgaaaga	cactttcttt	720
cttcaactctg	aagtagctgg	tggt				744

&lt;210&gt; 229

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 229

cgagtctggg	ttttgtctat	aaagtttgat	ccctcctttt	ctcatccaaa	tcattgtgaac	60
cattacacat	cgaaataaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgcagggttg	ttgtttttta	attattattg	ttagaaacgt	caccacagct	ccctgttaat	180
ttgtatgtga	cagccaactc	tgagaaggtc	ctatttttcc	acctgcagag	gatccagtct	240
cactaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

&lt;210&gt; 230

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 230

cagcagaaca	aatacaaaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
gagcgacagt	tcaaggagga	gaagcttgca	gagcagctca	agcaagctga	ggagctcagg	120
caatataaag	tcttggttca	cactcaggaa	cgagagctga	cccagttaag	ggagaagttg	180
cgggaaggga	gagatgcctc	cctctcattg	aatgagcctc	tccaggccct	cctcactccg	240
gatgaaccgg	acaagtccca	ggggcaggac	ctccaagaaa	cagacctcgg	cgcgcaccac	300
g						301



<210> 231  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 231  
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 caggaactcc aagtccacat ccttggaac tggggacttg cgcaggtag ccttgaggat 120  
 ggcaacacgg gacttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg 180  
 tctgaggatg gcaggatcaa tgatgtcagg ccggttggtg ccgccaatga tgaacacatt 240  
 tttttttgtg gacatgccat ccatttctgt caggatctgg ttgatgactc ggtcagcagc 300  
 c 301

<210> 232  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 232  
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 ggcgacagcg gggcttctctg attctggaat ataactttgt gttaaattaac agccacctat 120  
 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtctgtcca 180  
 cgtgctgtac caagtgtctg tgccagcctg ttacctgttc tctactgaaa tctggctaatt 240  
 gctcttctgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300  
 g 301

<210> 233  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 233  
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 cctagaagtt acagagcatc tagctggtgc gctggcacc cttggcctcac acagactccc 180  
 gagtagctgg gactacaggc acacagtcac tgaagcaggg cctgttagca attctatgcg 240  
 taaaaattaa catgagatga gtagagactt tattgagaaa gcaagagaaa atcctatcaa 300  
 c 301

<210> 234  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 234  
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 cattttattc atcatgatgc tttcttttctg ttcttctttt cgttttcttc ttttctttt 120  
 tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180  
 cgctcatga cagcaagttc aatgtttttg ccacctgact gaaccacttc caggagtgcc 240  
 ttgatcacca gcttaatggt cagatcatct gcttcaatgg cttcgtcagt atagttcttc 300  
 t 301

<210> 235  
 <211> 283  
 <212> DNA  
 <213> Homo sapien

&lt;400&gt; 235

tggggctgtg catcaggcgg gtttgagaaa tattcaattc tcagcagaag ccagaatttg	60
aattccctca tcttttaggg aatcatttac caggtttgga gaggattcag acagctcagg	120
tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata	180
atgttatctt tgaactgatg ctcataggag agaataaag aactctgagt gatatcaaca	240
ttagggattc aaagaaatat tagatttaag ctcacactgg tca	283

&lt;210&gt; 236

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 236

aggtcctcca ccaactgcct gaagcacggt taaaattggg aagaagtata gtgcagcata	60
aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg	120
tcggagcagc atcattaata ccaagcagaa tgcgtaatag ataaatacaa tgggtatatag	180
tgggtagacg gcttcatgag tacagtgtac tgtgggtatcg taatctggac ttggggttgta	240
aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc	300
a	301

&lt;210&gt; 237

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 237

cagtggtagt ggtgggtggac gtggcggttg tegtgggtgcc ttttttggtg cccgtcacaa	60
actcaatttt tgttgcgtcc tttttggcct tttccaattt gtccatctca attttctggg	120
ccttggtctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatatcct	180
ttgggtagtt ggtgccaaagc tcgtcaatgg cacagaatgg atcagcttct cgtaaatacta	240
gggttccgaa attcttttct cctttggata atgtagttca tatccattcc ctcctttatc	300
t	301

&lt;210&gt; 238

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 238

gggcagggtt tttttttttt ttttttgatg gtgcagaccc ttgctttatt tgtctgactt	60
gttcacagtt cagccccctg ctcagaaaac caacggggcca gctaaggaga ggaggaggca	120
ccttgagact tccggagtgc aggcctctcca gggttcccca gcccatcaat cattttctgc	180
accccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca	240
gtgtgggacc cagggctctg tcttcacagt aggaggtgga agggatgact aatttcttta	300
t	301

&lt;210&gt; 239

&lt;211&gt; 239

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 239

ataagcagct aggggaattct ttatttagta atgtcctaac ataaaagtcc acataactgc	60
ttctgtcaaa ccatgatact gagctttgtg acaaccaga aataactaag agaaggcaaa	120
cataatacct tagagatcaa gaaacattta cacagttcaa ctgtttaaaa atagctcaac	180
attcagccag tgagtagagt gtgaatgcc a gcatacacag tatacaggtc cttcaggga	239

&lt;210&gt; 240

<211> 300  
 <212> DNA  
 <213> Homo sapien

<400> 240  
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 gggatctgcc ctccagtga accttttaag gaagaagtgg gccaagcta agttccacat 120  
 gctgggtgag ccagatgact tctgttcctt ggtcactttc ttcaatgggg cgaatggggg 180  
 ctgccaggtt tttaaaatca tgcttcact tgaagcacac ggtcacttca ccctcctcac 240  
 gctgtgggtg tactttgatg aaaataccca ctttgttggc ctttctgaag ctataatgtc 300

<210> 241  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 241  
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 ctccctccatg tattggaaaa ctgcaaactg gactcaactg gaaggaagtg ctgctgccag 180  
 tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtcttttct 240  
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 g 301

<210> 242  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 242  
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 tgtggcattt cctcattttc tacattgtag aatcaagagt gttaaataaat gtatatcgat 120  
 gtcttcaaga atatatcatt cctttttcac tagaaccat tcaaaatata agtcaagaat 180  
 cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta 240  
 taagtaccca aagttttata aatcaaaaagc cctaattgata accattttta gaattcaatc 300  
 a 301

<210> 243  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 243  
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 tgacgtgcag tcggactctg tggcccaagg gtatggctct ctcggcatga tgaccagcg 180  
 gctggtttgt ccagatggca agacagtaga agcagaggct gccacggga ctgtaaccgg 240  
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 t 301

<210> 244  
 <211> 300  
 <212> DNA  
 <213> Homo sapien

<400> 244  
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ccagggacct tggaaacagt tgacactgta aggtgcttgc tccccaagac acatcctaaa	180
aggtgttgta atgggtgaaaa cgtcttcctt ctttattgcc ccttcttatt tatgtgaaca	240
actgtttgtc ttttgtgtat cttttttaa ctgtaaagtt caattgtgaa aatgaatc	300

<210> 245  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 245	
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aaggccagga gatattgtca ttaatgtara cttcaggaca ctagagtata gcagccctat	180
gttttcaaag agcagagatg caattaaata ttgttttagca tcaaaaaggc cactcaatac	240
agctaataaa atgaaagacc taatttctaa agcaattctt tataatttac aaagttttaa	300
g	301

<210> 246  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 246	
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acctgggctt attttaaaga actatttcta gctcagattg gtttccctat ggctaaaata	120
agtgccttct gtgaaaatta aataaaacag ttaattcaaa gccttgatat atgttaccac	180
taacaatcat actaaatata ttttgaagta caaagtttga catgctctaa agtgacaacc	240
caaatgtgtc ttacaaaaca cgttccctaac aaggtatgct ttacactacc aatgcagaaa	300
c	301

<210> 247  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 247	
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gcctaagagg gcgactggcg gcagcacaac caaggaaggc aagggttgtt cccccacgt	120
gtgtcctgtg ttcaggtgcg acacacaatc ctcatgggaa caggatcacc catgcgctgc	180
ccttgatgat caaggttggg gcttaagtgg attaaggag gcaagttctg ggttccttgc	240
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a	301

<210> 248  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 248	
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acaggaagaa agtggtttgg aagacagcca aagaaataaa agcagattaa attgtatcag	180
gtacattcca gcctgttggc aactccataa aaacatttca gattttaate ccgaatttag	240
ctaagagac tggatttttg ttttttatgt tgtgtgtcgc agagctaaaa actcagttcc	300
c	301

<210> 249  
 <211> 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 249

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ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgtcccggcc    120
ccaggggagac acagcagtga ctcagagctg gtcgcacact gtgcctccct cctcaccgcc    180
catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag    240
actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt    300
a                                                                 301

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&lt;210&gt; 250

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 250

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ggctctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacacttctc    60
cttatcttta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc    120
cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac    180
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta    240
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc    300
a                                                                 301

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&lt;210&gt; 251

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 251

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gccgaggtcc tacatttggc ccagtttccc cctgcaccc ctcaggggcc cctgcctcat    60
agacaacctc atagagcata ggagaactgg ttgccctggg ggcaggggga ctgtctggat    120
ggcagggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct    180
cattggggtc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccgaa    240
cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatcct    300
c                                                                 301

```

&lt;210&gt; 252

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 252

```

gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgtgg catttcctca    60
ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata    120
tcattccttt ttcactagga acccattcaa aatataagtc aagaatctta atatcaacaa    180
atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag taccctaaagt    240
tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc    300
a                                                                 301

```

&lt;210&gt; 253

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 253

```

ttccctaaga agatgttatt ttgttggggt ttgttccccc tccatctcga ttctcgtaac    60
caactaaaaa aaaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctccttagct    120

```

tggtctgatt gttttcagac cttaaaatat aaacttgttt cacaagcttt aatccatgtg 180  
gatttttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt 240  
tccatagtgc ccacagggtg ttcctcacat tttctccata ggaaaatgct ttttcccaag 300  
g 301

<210> 254  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 254  
cgctgcgcct ttccttgagg ggaggggcaa ggccagaggg ggtccaagtg cagcacgagg 60  
aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaaatcccc 120  
ccaaatctct tcatcttacc ctggtggact cctgactgta gaattttttg gttgaaacaa 180  
gaaaaaata aagcttttga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc 240  
acttaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc 300  
t 301

<210> 255  
<211> 302  
<212> DNA  
<213> Homo sapien

<400> 255  
agcttttttt tttttttttt tttttttttt ttcattaaaa aatagtgtc tttattataa 60  
attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat 120  
tggtattttt ttgagttctt caagcatctc ctaataccct caagggcctg agtagggggg 180  
aggaaaaagg actggagggtg gaatctttat aaaaaacaag agtgattgag gcagattgta 240  
aacattatta aaaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac 300  
aa 302

<210> 256  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)... (301)  
<223> n = A,T,C or G

<400> 256  
gttccagaaa acattgaagg tggttccca aagtctaact agggataccc cctctagcct 60  
aggaccctcc tccccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc 120  
acccccaaaa gcctggacac cttgagcaca cagttatgac caggacagac tcatctctat 180  
aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt 240  
gtggcctctc ggctgggtta gcaagaacat tcagggtagg cctaagttan tcgtgttagt 300  
t 301

<210> 257  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 257  
gttgtggagg aactctggct tgctcattaa gtccactga ttttactat cccctgaatt 60  
tccccactta tttttgtctt tcaactatgc aggccttaga agaggctac ctgcctccag 120  
tcttacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat 180

gtcacattac tcccttcagt gattttcttgt agaagtgcc atccctgaat gccaccaaga 240  
 tcttaatctt cacatcttta atcttatctc tttgactcct ctttacaccg gagaaggctc 300  
 c 301

<210> 258  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 258  
 cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc 60  
 agggggccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc 120  
 cccaggggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg 180  
 atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat 240  
 tggtgatccc tgggagcgcc ggtggagtaa cgttgggtcca tggaaagcag cgcccacaac 300  
 t 301

<210> 259  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 259  
 tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg 60  
 gtgtectgaa gtgatttgga cccctgaggg cagacaccta agtaggaatc ccagtgggaa 120  
 gcaaagccat aaggaagccc aggattcctt gtgatcagga agtggggccag gaaggctctgt 180  
 tccagctcac atctcatctg catgcagcac ggaccgatg cgcccactgg gtcttggctt 240  
 ccctcccatc ttctcaagca gtgtccttgt tgagccattt gcatccttgg ctccagggtg 300  
 c 301

<210> 260  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 260  
 ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaa at aagcaatggt 60  
 aaggtgtctt aacttgaaaa agattaggag tcaactggttt acaagttata attgaatgaa 120  
 agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaaca caggattaac 180  
 tagggcaaaa taaataagtg tgtggaagcc ctgataagtg ctttaataaac agactgattc 240  
 actgagacat cagtacctgc ccgggcgggc gctcgagccg aattctgcag atatccatca 300  
 c 301

<210> 261  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

## &lt;400&gt; 261

aaatattcga gcaaatcctg taactaatgt gtctccataa aaggctttga actcagtga	60
tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaaggtt	120
agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aaggttcaat	180
ggtgacatcc aatttcttct gataatttag attcctcaca accttcctag ttaagtgaag	240
ggcatgatga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc	300
a	301

&lt;210&gt; 262

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

## &lt;400&gt; 262

gaggagagcc tggtacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc	60
tgtagagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaattc ctgagtcacc	120
cctagacttc ctaaacacaga tcctctgggg ctggaacctg gcaactctgca tttgtaatga	180
gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtcccc	240
catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat	300
c	301

&lt;210&gt; 263

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (301)

&lt;223&gt; n = A,T,C or G

## &lt;400&gt; 263

tttagcttgt ggtaaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg	60
aaaattacta cttaatccta attcacaata acaatggcat taaggtttga cttgagttgg	120
ttcttagtat tatttatggt aaataggctc ttaccacttg caaataactg gccacatcat	180
taatgactga cttcccagta aggtctctta aggggtaagt angaggatcc acaggatttg	240
agatgctaag gccccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg	300
g	301

&lt;210&gt; 264

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

## &lt;400&gt; 264

aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaaacc	60
aatgaatgac tctaaaaaca atatttacat ttaatggttt gtagacaata aaaaaacaag	120
gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag	180
ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac	240
acccttcata taaattcact atcttggctt gaggcactcc ataaaatgta tcacgtgcac	300
a	301

&lt;210&gt; 265

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

## &lt;400&gt; 265



tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcattcttgt	60
cttcttgtga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta	120
catattcttg gaagtctcta atcaactttt gttccatttg tttcatttct tcaggagggga	180
ttttcagttt gtcaacatgt tctctaacaa cacttgccca tttctgtaa gaatccaaag	240
cagttccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg	300
c	301

<210> 266  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 266	
taccgtctgc ctttctctcc atccaggcca tctgcgaatc tacatgggtc ctctatttcg	60
acaccagatc actctttcct ctaccacacag gcttgctatg agcaagagac acaacctcct	120
ctcttctgtg ttccagcttc ttttctgtt cttcccaccc cttaagttct attcctgggg	180
atagagacac caatacccat aacctctctc ctaagcctcc ttataaccca ggggtgcacag	240
cacagactcc tgacaactgg taaggccaat gaactgggag ctacagctg gctgtgcctg	300
a	301

<210> 267  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 267	
aaagagcaca ggccagctca gcctgccctg gccatctaga ctacagcctgg ctccatgggg	60
gttctcagtg ctgagtcctat ccaggaaaag ctacacctaga ctttctgagg ctgaatcttc	120
atcctcacag gcagcttctg agagcctgat attcctagcc ttgatgggtct ggagtaaagc	180
ctcattctga ttctctcct tcttttcttt caagtgggtc ttcttcacat cctctgttc	240
aattcgcttc agcttgtctg ctttagccct catttccaga agcttcttct ctttggcatc	300
t	301

<210> 268  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 268	
aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt tttcttctta	60
gatcttggga gagctggttc ttctaaggag aaggaggaag gacagatgta actttggatc	120
tcgaagagga agtctaattg aagtaattag tcaacgggtc ttgttttagac tcttggataa	180
tgctgggtgg ctacgtgagc ccttttggag aaagcaagta ttattcttaa ggagtaacca	240
cttccattg ttctactttc taccatcatc aattgtatat tatgtattct ttggagaact	300
a	301

<210> 269  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 269	
taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat	60
aaaattacct ttattcacac atctcaaac aattctgcaa attcttagtg aagtttaact	120
atagtcacag accttaata ttacattgt tttctatgtc tactgaaaat aagttcacta	180
ctttctgga tattctttac aaaatcttat taaaattcct ggtattatca ccccaatta	240
tacagtgga caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc	300
t	301

<210> 270  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 270  
 cattgaagag cttttgcgaa acatcagaac acaagtgcctt ataaaattaa ttaagcctta 60  
 cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga 120  
 gagcttgctg gtgcagtga tattggataa cactattcat ggccgaattg atcaagtcaa 180  
 ccaactcctt gaactggatc atcagaagaa ggggtgtgca cgatatactg cactagataa 240  
 tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggctt aacagaaaac 300  
 a 301

<210> 271  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 271  
 aaaaggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttctcatt 60  
 tttatagctc atcttttagg ttgatattca gttcatgctt cccttgctgt tcttgatcca 120  
 gaattgcaat cacttcatca gcctgtatc gctccaattc tctataaagt gggccaagg 180  
 tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt 240  
 tctctcctcc agatganaac tgatcatgcy cccacatttt gggttttata gaagcagtca 300  
 c 301

<210> 272  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 272  
 taaattgcta agccacagat aacaccaatc aatggaaca aatcactgtc ttcaaagtgc 60  
 ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120  
 tccaataatt cctcatgat gagcaagaaa aattctttgc gcaccctcc tgcattcaca 180  
 gcattcttct caacaaatat aaccttgagt ggttcttctt aatctatgtt ctttgtttct 240  
 ctaaggactt ccattgcac tctacaata ttttctctac gcaccactag aattaagcag 300  
 g 301

<210> 273  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 273  
 acatgtgtgt atgtgtatct ttgggaaaan aanaagacat cttgtttayt atttttttgg 60  
 agagangctg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactyga 120

```

gaaccgtcta aaaataaaaat ttaccatgtc dtatattcct tatagtatgc ttatttcacc 180
tlyttttctgt ccagagagag tatcagtgc ananatttma gggatgaamac atgmattggg 240
gggacttnty ttacngagm accctgcccc sgccgctcg makengantt ccgcsananc 300
t 301

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<210> 274

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 274

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cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg 60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa 120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttggt gaaaagtcca 180
tctaggtagt gttgcattct cgtcttctt tctgcagtag ataatgaggt aaccgaaggc 240
aattgtgctt cttttgataa gaagctttct tggcatatc aggaaattcc aganaaagtc 300
c 301

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<210> 275

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 275

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tcgggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg 60
gggtgaaatt ggccaacttt ctattaactt atgttggaac ttttgccacc aacagtaagc 120
tgcccttctt aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtggag 180
tcaagagact cccaggcctc agcgtacctg cccgggcggc cgctcgaagc cgaattctgc 240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttcgccctat 300
a 301

```

<210> 276

<211> 301

<212> DNA

<213> Homo sapien

<400> 276

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tgtacacata ctcaataaat aaatgactgc attgtgggtat tattactata ctgattatat 60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat 120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc 180
caatacatTT aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttTgtg 240
aaaactattc agtatgtttc ccttgcttca tgtctgagaa ggctctcctt caatggggat 300
g 301

```

<210> 277

<211> 301

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 277  
 ttgtgtgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag 60  
 atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg 120  
 gaatcatggc actcctgata ctttcccaa tcaacactct caatgcccc cctcgtcct 180  
 caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga 240  
 gttcnctgtc gattacatct gaccagtctc cttttccga agtcntccg ttcaatcttg 300  
 c 301

<210> 278  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 278  
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60  
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgta 120  
 cagtctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgc 180  
 aatgaacatc tcatgtgtgc tcacaatggt ctggcactat tataagtgtc tcacagggtt 240  
 tatgtgttct tctgaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300  
 c 301

<210> 279  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 279  
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60  
 gttatatcaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc 120  
 ttagaccttt acctccagc caccacacag tgcttgatat ttcagagtca gtcattgggt 180  
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240  
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300  
 a 301

<210> 280  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 280  
 ggtactggag ttttctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg 60  
 tagaaagggtg gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct 120

tgagaaaaaa	acctaagatt	agcccaggtg	gttgccctgta	acttcagttt	ttctgcctgg	180
gtttgatata	gttttagggt	ggggtagat	taagatctaa	attacatcag	gacaaagaga	240
cagactatta	actccacagt	taattaagga	ggtatgttcc	atgtttattt	gttaaagcag	300
t						301

<210> 281  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 281						
aggtacaaga	aggggaatgg	gaaagagctg	ctgctgtggc	attgttcaac	ttggatattc	60
gccgagcaat	ccaaatcctg	aatgaagggg	catcttctga	aaaaggagat	ctgaatctca	120
atgtggtagc	aatggcttta	tcgggttata	cggatgagaa	gaactccctt	tgagagagaa	180
tgtgtagcac	actgcgatta	cagctaaata	acccgtattt	gtgtgtcatg	tttgcatttc	240
tgacaagtga	aacaggatct	tacgatggag	ttttgtatga	aaacaaagt	gcagtacctc	300
g						301

<210> 282  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 282						
caggtactac	agaattaaaa	tactgacaag	caagtagttt	cttggcgtgc	acgaattgca	60
tccagaaccc	aaaaattaag	aaattcaaaa	agacattttg	tgggcacctg	ctagcacaga	120
agcgcagaag	caaagcccag	gcagaaccat	gctaacctta	cagctcagcc	tgacacagaag	180
cgcagaagca	aagcccaggc	agaaccatgc	taaccttaca	gctcagcctg	cacagaagcg	240
cagaagcaaa	gcccgagcag	aacatgctaa	ccttacagct	cagcctgcac	agaagcacag	300
a						301

<210> 283  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 283						
atctgtatac	ggcagacaaa	ctttatarag	tgtagagagg	tgagcgaaag	gatgcaaaaag	60
cactttgagg	gctttataat	aatatgctgc	ttgaaaaaaa	aaatgtgtag	ttgatactca	120
gtgcatctcc	agacatagta	aggggttgct	ctgaccaatc	aggtgatcat	tttttctatc	180
acttcccagg	ttttatgcaa	aaattttggt	aaattctata	atggtgatat	gcactcttta	240
ggaaacatat	acatttttaa	aaatctattt	tatgtaagaa	ctgacagacg	aatttgcttt	300
g						301

<210> 284  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 284						
caggtacaaa	acgctattaa	gtggcttaga	atttgaacat	ttgtggtott	tatttacttt	60
gcttcgtgtg	tgggcaaagc	aacatcttcc	ctaaatatat	attaccaaga	aaagcaagaa	120
gcagattagg	tttttgacaa	aacaaacagg	ccaaaagggg	gctgacctgg	agcagagcat	180
ggtgagaggc	aaggcatgag	agggcaagtt	tgttgtggac	agatctgtgc	ctactttatt	240
actggagtaa	aagaaaacaa	agttcattga	tgtcgaagga	tatatacagt	gtagaaatt	300
a						301

<210> 285

<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 285  
acatcaccat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc 60  
aatgatcatt agtgttttaa aaaaaaatact gaaaactcct tctgcatccc aatctctaac 120  
caggaaagca aatgctatctt acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180  
attaaatatg tctgacttct tttgagggtca cactgactagg caaatgctat ttacgatctg 240  
caaaagctgt ttgaagagtc aaagccccc a t t t t c t g g a c c t g t a a c a g 300  
t 301

<210> 286  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 286  
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaacttttgc 60  
tgtatattat ttttgccctta cagtggatca ttctagtagg aaaggacagt aagatttttt 120  
atcaaaatgt gtcattgccag taagagatgt tatattcttt tctcatttct tccccacca 180  
aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt 240  
gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt ttttcccttg 300  
t 301

<210> 287  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 287  
tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60  
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggg tagaaatatg 120  
aaatgatttg gttatgaacg cacagtttag gcagcagggc cagaatcctg accctctgcc 180  
ccgtggttat ctcctcccca gcttggtgc ctcagtgtat cacagtattc cattttgttt 240  
gttgcattgc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc 300  
t 301

<210> 288  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 288  
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60  
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa 120  
gatctttaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatac 180  
aaaagcatct gcttttgtga tttaatttag ctcactctgc cactggaaga atccaaacag 240  
tctgccttaa ttttggtatg atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300  
a 301

<210> 289  
<211> 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 289

```

ggtacactgt ttccatgcta tgtttctaca cattgctacc tcagtgtcc tggaaactta      60
gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg      120
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa      180
cgttctataa atgaatgtgc tgaagcaaag tgcccatggg ggccggcgaan aagagaaaga      240
tgtgttttgt tttggactct ctgtggtccc ttccaatgct gtgggtttcc aaccagnnga      300
a                                                                                   301

```

&lt;210&gt; 290

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 290

```

acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac      60
tgactgatct gttcatttct ctcacagctc ttaccccaa aagcttttcc accctaagtg      120
ttctgacctc ctttttcta ctcacagctc ttaccccaa aagcttttcc accctaagtg      180
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctagcagtgc      240
tgccttgaac aaaaacattt ctccatgtct ctttttcttc atgcctcaag taacagtgag      300
a                                                                                   301

```

&lt;210&gt; 291

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 291

```

caggtaccaa tttcttctat cctagaaaca ttctatttta tgttgttgaa acataacaac      60
tatatcagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc      120
tttactcttt tgtttatagg tgaatcacia aatgtatttt tatgtattct gtagttcaat      180
agccatggct gtttacttca tttaatttat ttagcataaa gacattatga aaaggcctaa      240
acatgagctt cacttcccca ctaactaatt agcatctggt atttcttaac cgtaatgcct      300
a                                                                                   301

```

&lt;210&gt; 292

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 292

```

accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc      60
tgtattaaat aatttttaag tttaaaagat aaaataccat cattttaa at gttggtattc      120
aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg      180
ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc      240
tcactacaca cacagacccc acagtcctat atgccacaaa cacatttcca taacttgaaa      300
a                                                                                   301

```

```

<210> 293
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 293
ggtaccaagt gctggtgcca gctgtgtacc tgttctcact gaaaagtctg gcta atgctc      60
ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcttagagc actgactgtt      120
aacacaaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt      180
gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg      240
ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gctcgagcat      300
g                                                                                   301

```

```

<210> 294
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 294
tgaccataa caatatacac tagctatctt ttttaactgtc catcattagc accaatgaag      60
attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag      120
tttaactata gtcacaganc ttaaataatc acattgtttt ctatgtctac tgaaaataag      180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc      240
cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt      300
t                                                                                   301

```

```

<210> 295
<211> 305
<212> DNA
<213> Homo sapien

```

```

<400> 295
gtactctttc tctccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta      60
cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac      120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga      180
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacagggtga attggatggt      240
tctcagaacc atttcaccca gacagcctgt ttctatcctg tttataaat tagtttggtg      300
tctct                                                                                   305

```

```

<210> 296
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 296
agggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct      60

```



```

cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg      120
attaataaga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac      180
tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt      240
tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg      300
c                                                                                   301

```

```

<210> 297
<211> 300
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(300)
<223> n = A,T,C or G

```

```

<400> 297
actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttgtgcta      60
aaggttttga aaaccttgaa ggagaatcat tttgacaaga agtacttaag agtctagaga      120
acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt      180
tccatcattg ggagtgcact ggccatccct caaaatttgt ctgggctggc ctgagtggtc      240
accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc aactggcggg      300

```

```

<210> 298
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 298
tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc cctccccgcg      60
ggcatctgag agacctggtg ttccagtgtt tctggaaatg ggtcccagtg cgcgcggctg      120
tgaagctctc agatcaatca cgggaagggc ctggcggttg tggccacctg gaaccacctt      180
gtcctgtctg ttacatttc actaycaggt tttctctggg cattacnatt tgttcccccta      240
caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcaggtggct ctcagcgagg      300
t                                                                                   301

```

```

<210> 299
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 299
gttttgagac ggagtttcac tcttgttgcc cagactggac tgcaatggca gggctctctgc      60
tactgcacc ctctgcctcc caggttcgag caattctcct gcctcagcct cccaggtagc      120
tggtattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg      180
gagtttcgcc atgttggtga gctgggtctc aactcctgac ctcaagcgac ctgcctgcct      240
cggcctccca aagtgtgtga attataggca tgagtcaaca cgcccagcct aaagatattt      300
t                                                                                   301

```

```

<210> 300
<211> 301
<212> DNA
<213> Homo sapien

```

&lt;400&gt; 300

attcagttttt atttgctgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga	60
tatgtcccac acccactggg aaaggctccc acctggctac ttctctatc agctgggtca	120
gctgcattcc acaaggttct cagcctaattg agtttacta cctgccagtc tcaaaactta	180
gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttgttac	240
tataaagcct gcctctaaca gtccttgctt cttcacacca atcccgagcg catcccccat	300
g	301

&lt;210&gt; 301

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 301

ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc	60
agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt	120
gggaactcac aaagaccctc agagctgaga caccacaaac agtgggagct cacaagacc	180
ctcagagctg agacacccac aacagtggga gctcacaaag accctcagag ctgagacacc	240
cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt	300
t	301

&lt;210&gt; 302

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 302

aggtacacat ttagcttggt gtaaatgact cacaaaactg attttaaaat caagttaatg	60
tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac	120
ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg	180
ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca	240
caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg	300
g	301

&lt;210&gt; 303

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 303

aggtaccaac tgtggaaata ggtagaggat catTTTTtct ttccatatca actaagttgt	60
atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac	120
tggctaattg aactaccgct tgcattgtaa aaatgggtgt ttgtgaaatg atcataggcc	180
agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc	240
catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac	300
c	301

&lt;210&gt; 304

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 304

acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgccta	60
tattagtttc agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc	120
cttttttagtg tatcatatca ggaatcatct cacattgggt tgtgccatta ctggtgcagt	180
gacttttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga	240

ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct 300  
c 301

<210> 305  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 305  
gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag 60  
cagggggaca gacctggaca gacacgttgt catttgcctgc tgtgggtagg aaaatgggag 120  
taaaggagga gaaacagata caaaatctcc aactcagtat taaggatttc tcatgcctag 180  
aatattggta gaaacaagaa tacattcata tggcaataaa ctaaccatgg tggaacaaaa 240  
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag 300  
a 301

<210> 306  
<211> 8  
<212> PRT  
<213> Homo sapien

<400> 306  
Val Leu Gly Trp Val Ala Glu Leu  
1 5

<210> 307  
<211> 637  
<212> DNA  
<213> Homo sapien

<400> 307  
acaggggratg aagggaaagg gagaggatga ggaagccccc ctgggggattt ggtttgggtcc 60  
ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa atagggggcac 120  
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt 180  
cacaccattg gtgagggagg gattaccacc ctgggggttat gaagatgggtt gaacacccca 240  
cacatagcac cggagatatg agatcaacag tttcttagcc atagagattc acagcccaga 300  
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg 360  
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacgggtgggg caaactctga 420  
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtga 480  
actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatatagag gaagtagcca 540  
ggtggggagcc tttccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg 600  
ttacagatac tggggcagca aataaaaactg aatcttg 637

<210> 308  
<211> 647  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(647)  
<223> n = A,T,C or G

&lt;400&gt; 308

acgattttca	ttatcatgta	aatcgggtca	ctcaaggggc	caaccacagc	tgggagccac	60
tgctcagggg	aagggttcata	tgggactttc	tactgcccac	ggttctatac	aggatataaa	120
ggngcctcac	agtatagatc	tggtagcaaa	gaagaagaaa	caaacactga	tctctttctg	180
ccacccctct	gacccttttg	aactcctctg	accctttaga	acaagcctac	ctaatactctg	240
ctagagaaaa	gaccaacaac	ggcctcaaag	gatctcttac	catgaaggtc	tcagctaatt	300
cttgggctaag	atgtgggttc	cacattagggt	tctgaatatg	gggggaaggg	tcaatttgct	360
catttttgtgt	gtggataaag	tcaggatgcc	caggggccag	agcagggggc	tgcttgcttt	420
gggaacaatg	gctgagcata	taaccatagg	ttatggggaa	caaaacaaca	tcaaagtcac	480
tgtatcaatt	gcatgaaga	cttgagggac	ctgaatctac	cgattcatct	taaggcagca	540
ggaccagttt	gagtggaac	aatgcagcag	cagaatcaat	ggaaacaaca	gaatgattgc	600
aatgtccttt	ttttctctct	gcttctgact	tgataaaagg	ggaccgt		647

&lt;210&gt; 309

&lt;211&gt; 460

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 309

actttatagt	ttaggctgga	cattggaaaa	aaaaaaaaagc	cagaacaaca	tgtgatagat	60
aatatgattg	gctgcacact	tccagactga	tgaatgatga	acgtgatgga	ctattgtatg	120
gagcacatct	tcagcaagag	ggggaaatac	tcatcatttt	tggccagcag	ttgtttgatc	180
accaaaccatc	atgccagaat	actcagcaaa	ccttcttagc	tcttgagaag	tcaaagtccg	240
ggggaattta	ttcctggcaa	ttttaattgg	actccttatg	tgagagcagc	ggctacccag	300
ctggggtggt	ggagcgaacc	cgtcactagt	ggacatgcag	tggcagagct	cctggtaacc	360
acctagagga	atacacaggc	acatgtgtga	tgccaagcgt	gacacctgta	gcactcaaat	420
ttgtcttggt	tttgtctttc	ggtgtgtaag	attcttaagt			460

&lt;210&gt; 310

&lt;211&gt; 539

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 310

acgggactta	tcaaataaag	ataggaaaag	aagaaaactc	aaatattata	ggcagaaatg	60
ctaaagggtt	taaaatatgt	caggattgga	agaaggcatg	gataaagaac	aaagttcagt	120
taggaaagag	aaacacagaa	ggaagagaca	caataaaaag	cattatgtat	tctgtgagaa	180
gtcagacagt	aagatttgtg	ggaaatgggt	tggtttgttg	tatggtatgt	attttagcaa	240
taatctttat	ggcagagaaa	gctaaaatcc	tttagcttgc	gtgaatgac	acttgctgaa	300
ttcctcaagg	taggcagatg	gaaggagggt	ttagaggaga	cacagacaca	atgaactgac	360
ctagatagaa	agccttagta	tactcagcta	ggaatagtga	ttctgagggc	acactgtgac	420
atgattatgt	cattacatgt	atggtagtga	tggggatgat	aggaaggaag	aacttatggc	480
atattttcac	ccccacaaaa	gtcagttaaa	tattgggaca	ctaaccatcc	aggtcaaga	539

&lt;210&gt; 311

&lt;211&gt; 526

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (526)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 311

caaatttgag	ccaatgacat	agaattttac	aaatcaagaa	gcttattctg	gggccatttc	60
ttttgacgtt	ttctctaaac	tactaaagag	gcattaatga	tccataaatt	atattatcta	120
catttacagc	atttaaaatg	tgttcagcat	gaaatattag	ctacagggga	agctaaataa	180

attaacatg	gaataaagat	ttgtccttaa	atataatcta	caagaagact	ttgatatttg	240
tttttcacaa	gtgaagcatt	cttataaagt	gtcataacct	ttttggggaa	actatgggaa	300
aaaatgggga	aactctgaag	ggttttaagt	atcttacctg	aagctacaga	ctccataaacc	360
tctctttaca	gggagctcct	gcagccccta	cagaaatgag	tggctgagat	tcttgattgc	420
acagcaagag	cttctcatct	aaaccctttc	ccttttttagt	atctgtgtat	caagtataaa	480
agttctataa	actgtagtnt	acttatttta	atccccaag	cacagt		526

&lt;210&gt; 312

&lt;211&gt; 500

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(500)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 312

cctctctctc	cccacccct	gactctagag	aactggggtt	tctcccagta	ctccagcaat	60
tcatttctga	aagcagttga	gccactttat	tccaaagtac	actgcagatg	ttcaaactct	120
ccatttctct	ttcccttcca	cctgccagtt	ttgctgactc	tcaacttgtc	atgagtgtaa	180
gcattaagga	cattatgctt	cttcgattct	gaagacagge	cctgctcatg	gatgactctg	240
gcttcttagg	aaaatatttt	tcttccaaaa	tcagtaggaa	atctaaactt	atccccctct	300
tgcagatgtc	tagcagcttc	agacatttgg	ttaagaaccc	atgggaaaaa	aaaaaatcct	360
tgctaattgt	gtttcctttg	taaaccanga	ttcttatttg	nctggatatag	aatatcagct	420
ctgaacgtgt	ggtaaagatt	tttgtgtttg	aatataggag	aaatcagttt	gctgaaaagt	480
tagtcttaat	tatctattgg					500

&lt;210&gt; 313

&lt;211&gt; 718

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(718)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 313

ggagatttgt	gtggtttgca	gccgaggag	accaggaaga	tctgcatggt	gggaaggacc	60
tgatgataca	gaggtgagaa	ataagaaagg	ctgctgactt	taccatctga	ggccacacat	120
ctgctgaaat	ggagataatt	aacatcacta	gaaacagcaa	gatgacaata	taatgtctaa	180
gtagtgacat	gtttttgcac	atttccagcc	cttttaaata	tccacacaca	caggaagcac	240
aaaaggaage	acagagatcc	ctgggagaaa	tgcccggccg	ccatcttggg	tcacgatga	300
gcctcgccct	gtgcctgntc	ccgcttggtg	gggaaggaca	ttagaaaatg	aattgatgtg	360
ttccttaaag	gatggcagga	aaacagatcc	tgttgtggat	atttatttga	acgggattac	420
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aactggggag	gagataccac	ggggcagagg	tcaggattct	ggccctgctg	cctaactgtg	600
cgttatacca	atcatttcta	tttctaccct	caaacaagct	gtngaataatc	tgacttacgg	660
ttcttntggc	ccacattttc	atnateccacc	ccntcntttt	aannttantc	caaantgt	718

&lt;210&gt; 314

&lt;211&gt; 358

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 314

```

gtttattttac attacagaaa aaacatcaag acaatgtata ctattttcaaa tatatccata      60
cataatcaaaa tatagctgta gtacatgttt tcattgggtg agattaccac aaatgcaagg      120
caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg tgtagtccaa      180
gctctcggtg gtccagccac tgtgaaacat gctcccttta gattaacctc gtggacgctc      240
ttgttgatt gctgaactgt agtgccctgt attttgcttc tgtctgtgaa ttctgttgct      300
tctggggcat ttccttgtga tgcagaggac caccacacag atgacagcaa tctgaatt      358

```

&lt;210&gt; 315

&lt;211&gt; 341

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 315

```

taccacctcc ccgctggcac tgatgagccg catcaccatg gtcaccagca ccatgaaggc      60
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gacccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag ccccaatgac      180
agtcaccagc tccccgacca gccggatata gtccttaggg gtcattgtagg cttcctgaag      240
tagcttctgc tgtaagaggg tgtgtcccg ggggctcgtg cggttattgg tcttgggctt      300
gagggggcgg tagatgcagc acatggtgaa gcagatgatg t      341

```

&lt;210&gt; 316

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 316

```

agactgggca agactcttac gccccacact gcaatttggt cttgttgccg tatccattta      60
tgtgggcctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact      120
cattcaggga gctctgggtg caatattagt t      151

```

&lt;210&gt; 317

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 317

```

agaactagtg gatcctaag aaataacctga aacatatatt ggcatttata aatggctcaa      60
atcttcattt atctctggcc ttaacctgg ctctgagggc tgcggccagc agatcccagg      120
ccagggtctt gttcttgcca cacctgcttg a      151

```

&lt;210&gt; 318

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 318

```

actggtggga ggcgtgttt agttggctgt tttcagaggg gtctttcgga gggacctcct      60
gctgcaggct ggagtgtctt tattcctggc gggagaccgc acattccact gctgaggctg      120
tgggggcggt ttatcaggca gtgataaaca t      151

```

&lt;210&gt; 319

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 319

```

aactagtggg tccagagcta taggtacagt gtgatctcag ctttgcaaac acattttcta      60
catagatagt actaggtatt aatagatatg taaagaaaga aatcacacca ttaataatgg      120

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<210> 320  
<211> 150  
<212> DNA  
<213> Homo sapien

<400> 320  
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gagcggctgc cctttttttt tttttttttg ggggggaatt tttttttttt aatagttatt 120  
gagtgttcta cagcttacag taaataccat 151

<210> 321  
<211> 151  
<212> DNA  
<213> Homo sapien

<400> 321  
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tagggtggca ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg 120  
tgcctctgag aaatcaaagt cttcatacac t 151

<210> 322  
<211> 151  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(151)  
<223> n = A,T,C or G

<400> 322  
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tttgggcttg gtcagtttgc cacagggctt ggagatggtg acagtcttct ggcattcggc 120  
attgtgcagg gctcgcttca nacttcagtt t 151

<210> 323  
<211> 151  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(151)  
<223> n = A,T,C or G

<400> 323  
tgaggacttg tktttctttt ctttattttt aatcctctta ckttgtaa atattgccta 60  
nagactcant tactaccag tttgtggtt twtgggagaa atgtaactgg acagttagct 120  
gttcaatyaa aaagacactt ancccatgtg g 151

<210> 324  
<211> 461  
<212> DNA  
<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(461)

<223> n = A,T,C or G

<400> 324

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agaagtgggc	agctaaagga	atccaggttg	ttgggtggac	tgtaataacc	tttgatgaaa	120
agagttacta	cgaatcccat	cttgggtcca	gctatatcac	tgacagcatg	gtagaagact	180
gcgaacctca	cttctagact	ttcacggtgg	gacgaaacgg	gttcagaaac	tgccaggggc	240
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cacacaaatg	caatagttgg	tcaactgcatt	tttacctgaa	ccaaagctaa	acccggtgtt	360
gccaccatgc	accatggcat	gccagagttc	aacactgttg	ctcttgaaaa	ttgggtctga	420
aaaaacgcac	aagagccctt	gccctgccct	agctgangca	c		461

<210> 325

<211> 400

<212> DNA

<213> Homo sapien

<400> 325

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gttttgtttt	ggactctctg	tggtcccttc	caatgctgtg	ggtttccaac	caggggaagg	300
gtcccttttg	cattgccaag	tgccataacc	atgagcacta	cgctaccatg	gttctgcctc	360
ctggccaagc	aggctggttt	gcaagaatga	aatgaatgat			400

<210> 326

<211> 1215

<212> DNA

<213> Homo sapien

<400> 326

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ctttccccta	gatccagaaa	taaagtctaa	gagaagcgca	aaaaaaaaaa	aaaaaaaaaa	1200
aaaaaaaaaa	aaaaa					1215

<210> 327

<211> 220



&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 327

```

Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met
 1           5           10           15
Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
          20           25           30
Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
          35           40           45
Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
          50           55           60
Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
65           70           75           80
Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
          85           90           95
Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
          100          105          110
Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
          115          120          125
Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
          130          135          140
Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
145          150          155          160
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
          165          170          175
Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
          180          185          190
Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
          195          200          205
Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
          210          215          220

```

&lt;210&gt; 328

&lt;211&gt; 234

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 328

```

cgctcgctctc tggtagctgc agccaaatca taaacggcga ggactgcagc ccgcactcgc      60
agccctggca ggcggcactg gtcattgaaa acgaattggt ctgctcgggc gtcctgggtgc      120
atccgcagtg ggtgctgtca gccacacact gtttccagaa ctctacacc atcgggctgg      180
gcctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag gcca      234

```

&lt;210&gt; 329

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 329

```

Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser
 1           5           10           15
Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu
          20           25           30
Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr
          35           40           45
His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
          50           55           60

```

Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala  
 65 70 75

<210> 330  
 <211> 70  
 <212> DNA  
 <213> Homo sapien

<400> 330  
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 gctgcagcca 70

<210> 331  
 <211> 22  
 <212> PRT  
 <213> Homo sapien

<400> 331  
 Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu  
 1 5 10 15  
 Val Ser Gly Ser Cys Ser  
 20

<210> 332  
 <211> 2507  
 <212> DNA  
 <213> Homo sapien

<400> 332  
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 gtacatcaac tgttcagctt cctgggaaag tagttgtggt cacaggagct aatacaggta 180  
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 gcttcttagc tgaggaaaag cacctccacg ttttgatcaa caatgcagga gtgatgatgt 420  
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&lt;210&gt; 333

&lt;211&gt; 3030

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 333

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&lt;210&gt; 334

&lt;211&gt; 2417

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 334

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&lt;211&gt; 2984

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 335

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 <212> PRT  
 <213> Homo sapien

<400> 336  
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 Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln  
 35 40 45  
 Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala  
 50 55 60  
 Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln  
 65 70 75 80  
 Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln  
 85 90 95  
 Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala  
 100 105 110  
 Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn  
 115 120 125  
 Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro  
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 Ala Phe Trp  
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<400> 338  
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 1 5

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 <211> 318  
 <212> PRT  
 <213> Homo sapien

<400> 339  
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 Leu Tyr Met Ala Ala Pro Gln Ile Arg Lys Met Leu Ser Ser Gly Val

<213> Homo sapien

**<400> 340**

<213> Homo sapien

&lt;400&gt; 341

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&lt;210&gt; 342

&lt;211&gt; 592

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 342

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&lt;210&gt; 343

&lt;211&gt; 382

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 343

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&lt;210&gt; 344

&lt;211&gt; 536

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 344

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&lt;210&gt; 345

&lt;211&gt; 251



&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 345

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gtgccatttc	c					251

&lt;210&gt; 346

&lt;211&gt; 282

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(282)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 346

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&lt;210&gt; 347

&lt;211&gt; 201

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(201)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 347

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&lt;210&gt; 348

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 348

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gccctgcctc	c					251

&lt;210&gt; 349

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 349

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&lt;210&gt; 350

&lt;211&gt; 908

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 350

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&lt;210&gt; 351

&lt;211&gt; 472

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 351

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&lt;210&gt; 352

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 352

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<210> 353  
 <211> 436  
 <212> DNA  
 <213> Homo sapien

<400> 353  
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<210> 354  
 <211> 854  
 <212> DNA  
 <213> Homo sapien

<400> 354  
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 <211> 676  
 <212> DNA  
 <213> Homo sapien

<400> 355  
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<210> 356

<211> 574  
 <212> DNA  
 <213> Homo sapien

<400> 356

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<210> 357  
 <211> 393  
 <212> DNA  
 <213> Homo sapien

<400> 357

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<210> 358  
 <211> 630  
 <212> DNA  
 <213> Homo sapien

<400> 358

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<210> 359  
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 <212> DNA  
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<400> 359

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&lt;210&gt; 360

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 360

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&lt;210&gt; 361

&lt;211&gt; 351

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 361

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&lt;210&gt; 362

&lt;211&gt; 463

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 362

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&lt;210&gt; 363

&lt;211&gt; 653

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(653)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 363

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&lt;210&gt; 364

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 364

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&lt;210&gt; 365

&lt;211&gt; 356

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 365

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&lt;210&gt; 366

&lt;211&gt; 1851

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 366

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&lt;210&gt; 367

&lt;211&gt; 668

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 367

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&lt;210&gt; 368

&lt;211&gt; 1512

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 368

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&lt;210&gt; 369

&lt;211&gt; 1853

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 369

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&lt;210&gt; 370

&lt;211&gt; 2184

&lt;212&gt; DNA



&lt;213&gt; Homo sapien

&lt;400&gt; 370

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&lt;210&gt; 371

&lt;211&gt; 1855

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

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&lt;400&gt; 371

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&lt;211&gt; 1059

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 372

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&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 373

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&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 374

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Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
65              70              75              80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
              85              90              95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
              100              105              110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
              115              120              125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
              130              135              140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
145              150              155              160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
              165              170              175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
              180              185              190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
              195              200              205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
              210              215              220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
225              230              235              240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
              245              250              255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
              260              265              270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
              275              280              285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
              290              295              300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
305              310              315              320
Ser Met Leu Phe Leu Val Ile Ile Met
              325

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&lt;210&gt; 377

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(148)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 377

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Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile
1              5              10              15
Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
              20              25              30
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
              35              40              45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
              50              55              60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
65              70              75              80
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
              85              90              95

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Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro  
 100 105 110  
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp  
 115 120 125  
 Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser  
 130 135 140  
 Lys Asn Lys Val  
 145

<210> 378  
 <211> 1719  
 <212> PRT  
 <213> Homo sapien

<400> 378  
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
 1 5 10 15  
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
 20 25 30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val

340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Asn Val Ser Arg Thr Arg Asn Lys  
 370 375 380  
 Pro Arg Thr His Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser  
 385 390 395 400  
 Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys  
 405 410 415  
 Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly  
 420 425 430  
 Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys  
 435 440 445  
 Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly  
 450 455 460  
 Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys  
 465 470 475 480  
 Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys  
 485 490 495  
 Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp  
 500 505 510  
 Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu  
 515 520 525  
 Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp  
 530 535 540  
 Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln  
 545 550 555 560  
 Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val  
 565 570 575  
 Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn  
 580 585 590  
 Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu  
 595 600 605  
 Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp  
 610 615 620  
 Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys  
 625 630 635 640  
 Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys  
 645 650 655  
 Asn Lys His Gly Leu Thr Pro Leu Leu Gly Val His Glu Gln Lys  
 660 665 670  
 Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala  
 675 680 685  
 Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly  
 690 695 700  
 Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser  
 705 710 715 720  
 Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser  
 725 730 735  
 His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln  
 740 745 750  
 Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys  
 755 760 765  
 Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser  
 770 775 780  
 Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp  
 785 790 795 800  
 Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly

805 810 815  
 Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn  
 820 825 830  
 Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe  
 835 840 845  
 Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser  
 850 855 860  
 Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn  
 865 870 875 880  
 Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Ser Gln Arg Leu  
 885 890 895  
 Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile  
 900 905 910  
 Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn  
 915 920 925  
 Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro  
 930 935 940  
 Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu  
 945 950 955 960  
 Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe  
 965 970 975  
 Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His  
 980 985 990  
 Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser  
 995 1000 1005  
 Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu  
 1010 1015 1020  
 Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His  
 1025 1030 1035 1040  
 Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met  
 1045 1050 1055  
 Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met  
 1060 1065 1070  
 Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys  
 1075 1080 1085  
 Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr  
 1090 1095 1100  
 Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys  
 1105 1110 1115 1120  
 Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp  
 1125 1130 1135  
 Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His  
 1140 1145 1150  
 Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp  
 1155 1160 1165  
 Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg  
 1170 1175 1180  
 Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val  
 1185 1190 1195 1200  
 Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys  
 1205 1210 1215  
 Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly  
 1220 1225 1230  
 Asn Ser Glu Val Val Lys Leu Leu Asp Arg Arg Cys Gln Leu Asn  
 1235 1240 1245  
 Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys  
 1250 1255 1260  
 Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro



1265                      1270                      1275                      1280  
 Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr  
                                  1285                      1290                      1295  
 Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp  
                                  1300                      1305                      1310  
 Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val  
                                  1315                      1320                      1325  
 His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala  
                                  1330                      1335                      1340  
 Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala  
 1345                      1350                      1355                      1360  
 Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn  
                                  1365                      1370                      1375  
 Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr  
                                  1380                      1385                      1390  
 Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr  
                                  1395                      1400                      1405  
 Lys Glu Lys Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu  
                                  1410                      1415                      1420  
 Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly  
 1425                      1430                      1435                      1440  
 Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn  
                                  1445                      1450                      1455  
 Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser  
                                  1460                      1465                      1470  
 Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly  
                                  1475                      1480                      1485  
 Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu  
                                  1490                      1495                      1500  
 Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys  
 1505                      1510                      1515                      1520  
 Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser  
                                  1525                      1530                      1535  
 Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu  
                                  1540                      1545                      1550  
 Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser  
                                  1555                      1560                      1565  
 Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe  
                                  1570                      1575                      1580  
 Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe  
 1585                      1590                      1595                      1600  
 Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly  
                                  1605                      1610                      1615  
 Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro  
                                  1620                      1625                      1630  
 Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln  
                                  1635                      1640                      1645  
 Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile  
                                  1650                      1655                      1660  
 Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser  
 1665                      1670                      1675                      1680  
 Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn  
                                  1685                      1690                      1695  
 Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr  
                                  1700                      1705                      1710  
 Met Lys His Gln Ser Gln Leu  
                                  1715

<210> 379  
 <211> 656  
 <212> PRT  
 <213> Homo sapien

<400> 379  
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
 1 5 10 15  
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
 20 25 30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu  
 370 375 380  
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys  
 385 390 395 400  
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu  
 405 410 415

Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn  
 420 425 430  
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro  
 435 440 445  
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu  
 450 455 460  
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu  
 465 470 475 480  
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp  
 485 490 495  
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu  
 500 505 510  
 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys  
 515 520 525  
 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly  
 530 535 540  
 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser  
 545 550 555 560  
 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr  
 565 570 575  
 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln  
 580 585 590  
 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln  
 595 600 605  
 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys  
 610 615 620  
 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile  
 625 630 635 640  
 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu  
 645 650 655

&lt;210&gt; 380

&lt;211&gt; 671

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 380

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
 1 5 10 15  
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
 20 25 30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala

165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu  
 370 375 380  
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys  
 385 390 395 400  
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu  
 405 410 415  
 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn  
 420 425 430  
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro  
 435 440 445  
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu  
 450 455 460  
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu  
 465 470 475 480  
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp  
 485 490 495  
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu  
 500 505 510  
 Asn Gly Gln Pro Glu Lys Arg Ser Gln Glu Pro Glu Ile Asn Lys Asp  
 515 520 525  
 Gly Asp Arg Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys Lys  
 530 535 540  
 His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly Ala  
 545 550 555 560  
 Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser Arg  
 565 570 575  
 Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr His  
 580 585 590  
 Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn  
 595 600 605  
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile  
 610 615 620  
 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys

625		630		635		640
Glu Lys Asp Ile Leu	His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala					
	645		650		655	
Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu						
	660		665		670	

<210> 381  
 <211> 251  
 <212> DNA  
 <213> Homo sapien

<400> 381  
 ggagaagcgt ctgctggggc aggaaggggt ttccctgcc tctcacctgt ccctcaccaa 60  
 ggtaacatgc ttcccctaag ggtatcccaa cccaggggcc tcaccatgac ctctgagggg 120  
 ccaatatccc aggagaagca ttggggaggt gggggcaggt gaaggacca ggactcacac 180  
 atcctgggcc tccaaggcag aggagaggggt cctcaagaag gtcaggagga aaatccgtaa 240  
 caagcagtca g 251

<210> 382  
 <211> 3279  
 <212> DNA  
 <213> Homo sapiens

<400> 382  
 ctctctgcag ccccatgct ggtgaggggc acgggcagga acagtggacc caacatggaa 60  
 atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt 120  
 cactgggagg ggacatcctg cagaaggtag gagtgcagaa acacccgctg caggggaggg 180  
 gagagccctg cggcacctgg gggagcagag ggagcagcac ctgcccaggc ctgggaggag 240  
 gggcctggag ggcgtgagga ggagcgaggg ggctgcatgg ctggagttag ggatcagggg 300  
 cagggcgcga gatggcctca cacaggggaag agagggcccc tctgcaggg cctcacctgg 360  
 gccacaggag gacactgctt ttcctctgag gagttaggag ctgtggatgg tgctggacag 420  
 aagaaggaca gggcctggct cagggtgtcca gaggtgtctg ctggcttccc tttgggatca 480  
 gactgcaggg agggagggcg gcaggggtgt ggggggagtg acgatgagga tgacctgggg 540  
 gtggctccag gccttgcctc tgccctgggc ctcaaccagc ctccctcaca gtctcctggc 600  
 cctcagtctc tccctccac tccatcctcc atctggcctc agtgggtcat tctgatcact 660  
 gaactgacca taccagccc tgcccacggc cctccatggc tcccaatgc cctggagagg 720  
 ggacatctag tcagagagta gtccctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780  
 gcatectgca gatgggtccc gccctcatcc tgctgacctg tctgcaggga ctgtcctcct 840  
 ggaccttgcc ccttgctgag gagctggacc ctgaagtccc ctcccatag gccaaactg 900  
 gagccttggt cctctgttg gactcctgc ccatattctt gtgggagtgg gttctggaga 960  
 catttctgtc tgttctctgag agctgggaat tgctctcagt catctgcctg cgcggttctg 1020  
 agagatggag ttgcctaggc agttattggg gccaatcttt ctactgtgt ctctcctcct 1080  
 ttacccttag ggtgattctg ggggtccact tgtctgtaat ggtgtgcttc aaggtatcac 1140  
 atcatggggc cctgagccat gtgccctgcc tgaaaagcct gctgtgtaca ccaaggtgg 1200  
 gcattaccgg aagtggatca aggacacat cgcagccaac ccctgagtgc ccctgtccca 1260  
 ccctacctc tagtaaattt aagtccacct cacgttctgg catcacttg cctttctgga 1320  
 tgctggacac ctgaagcttg gaactcacct ggccgaagct cgagcctcct gactcctact 1380  
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 cgtcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtgg 1920  
 ttattatggg ttgttacatt gataggatac atactgaaat cagcaaaca aacagatgta 1980  
 tagattagag tgtggagaaa acagaggaaa acttgcagtt acgaagactg gcaacttggc 2040

```

tttactaagt tttcagactg gcaggaagtc aaacctatta ggctgaggac cttgtggagt 2100
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gcatatccga cagttattct ctccaagtgg agacttacgg acagcatata attctccctg 2220
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cccagctgat agaggaagta gccaggtggg agcctttccc agtgggtgtg ggacatatct 3180
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gttttcagac cttaaaaaaa aaaaaaaaaa aaaagtgtt 3279

```

&lt;210&gt; 383

&lt;211&gt; 154

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 383

```

Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
      5                      10                      15

Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
      20                      25                      30

His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35                      40                      45

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50                      55                      60

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65                      70                      75                      80

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
      85                      90                      95

Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
      100                     105                     110

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
      115                     120                     125

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
      130                     135                     140

Ala Leu Glu Arg Gly His Leu Val Arg Glu
      145                     150

```

<210> 384  
 <211> 557  
 <212> DNA  
 <213> Homo sapiens

<400> 384  
 ggatcctcta gagcgccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60  
 aaagatgtgt tttgttttg actctctgtg gtcccttcca atgctgtggg tttccaacca 120  
 ggggaagggt cccttttgca ttgccaaagt ccataaccat gaggactact ctaccatggg 180  
 tctgcctcct ggccaagcag gctgggttg aagaatgaaa tgaatgattc tacagctagg 240  
 acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300  
 ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360  
 tccccagac acatcctaaa aggtgttgta atgggtgaaa cgtcttcctt ctttattgcc 420  
 ccttccttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480  
 tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttcc aaagtaaaaa 540  
 aaaaaaaaa aaaaaaa 557

<210> 385  
 <211> 337  
 <212> DNA  
 <213> Homo sapiens

<400> 385  
 ttcccagggt atgtgcgagg gaagacacat ttactatcct tgatggggct gattccttta 60  
 gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120  
 tctcaaagcc atctgctgtc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180  
 aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240  
 tatcagacag gtccagtttc cgcaccaaca cctgctgggt ccctgtcgtg gtctggatct 300  
 ctttggccac caattcccc tttccacat ccggca 337

<210> 386  
 <211> 300  
 <212> DNA  
 <213> Homo sapiens

<400> 386  
 gggcccgcta cgggccagg cccgcctcg cgagtcctcc tccccgggtg cctgccccga 60  
 gccgcctcgg ccagagggt gggcgcgagg ctgcctctac cggctggcgg ctgtaactca 120  
 gcgaccttgg ccgaaggct cttagcaagg cccaccgacc ccagccgagg cggcgaggcg 180  
 gcggaacttt cccggtgtgt ggggaggagc ggactgcgtg tccgaggagc ggcagcgaag 240  
 atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

<210> 387  
 <211> 537  
 <212> DNA  
 <213> Homo sapiens

<400> 387  
 gggccgagtc gggcaccaag ggactctttg caggcttctt tctcggatc atcaaggctg 60  
 cccctccttg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120  
 tgaaccagga cgggcttctg ggcggtgaa aggggcaagg aggcaaggac cccgtctctc 180  
 ccacggatgg ggagagggca ggaggagacc cagccaagtg ccttttcttc agcactgagg 240  
 gagggggctt gtttcccttc cctcccggcg acaagctcca gggcagggtg gtccctctgc 300  
 gcggcccagc acttctcag acacaacttc ttctgctgc tccagtcgtg gggatcatca 360  
 cttacccacc ccccaagttc aagaccaa atctccagctg ccccttctgt gtttccctgt 420  
 gtttgcgtga gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg ttagtctctc 480  
 ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaaa aaaaaaa 537

<210> 388  
<211> 520  
<212> DNA  
<213> Homo sapiens

<400> 388  
aggataattt ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60  
tgagggttaaa ccagtttgca tcccccta atgtggaaaaag taagaggact actcagcact 120  
gtttgaagat tgcctcttct acagcttctg agaatttgtt tatttcactt gccaaagtga 180  
ggacccccct cccaacatgc cccagccccc ccctaagcat ggtcccttgt caccaggcaa 240  
ccaggaaact gctacttgtg gacctcacca gagaccagga gggtttggtt agctcacagg 300  
acttccccca cccagaaga ttagcatccc atactagact cataactcaac tcaactaggc 360  
tcataactcaa ttgatgggta ttagacaatt ccatttcttt ctggttatta taaacagaaa 420  
atctttcttc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480  
atgaacttgt cttattttaa tgggggggtt ttttcttgtt 520

<210> 389  
<211> 365  
<212> DNA  
<213> Homo sapiens

<400> 389  
cgttgcccc gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60  
gagttaaggc tggatttcag atctgcctgg ttccagccgc agtggtgccct ctgctcccc 120  
aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180  
aagcctatgg ccagctgtct ttgtgttccc tctcaccgc ctgtcctcac agctgagact 240  
cccaggaaac cttcagacta ccttcctctg ccttcagcaa ggggcgttgc ccacattctc 300  
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gggag 365

<210> 390  
<211> 221  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(221)  
<223> n = A,T,C or G

<400> 390  
tgctctcca tcttgcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60  
tacacggntt ctcattgggtg tggaacatct ctgcttgagg ttccaggaag gcctctggct 120  
gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180  
tcaaagtcta gagggagtgg aggagttaag gctggatttc a 221

<210> 391  
<211> 325  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(325)  
<223> n = A,T,C or G

<400> 391



```

tggagcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagccagggc actgctgcc aacagccagtc cnnataccat catgtnaccc ggtgngctct 180
naanttngat ntccanagcc ctaccccatcn tagttctgct ctcccacccg ntaccagccc 240
cactgcccag gaatcctaca gccagtaccc tgtcccagcg tctctaccta ccagtacgat 300
gagacctccg gctactacta tgacc                                     325

```

&lt;210&gt; 392

&lt;211&gt; 277

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(277)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 392

```

atattgttta actccttctt ttatatcttt taacattttc atggngaaa gttcacatct 60
agtctcactt nggcnagnn ctctactctg agtctcttcc ccggcctggn ccagtnagna 120
antaccanga accgncatgn cttaanaacn ncctggtttn tgggttnntc aatgactgca 180
tgcagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa                                     277

```

&lt;210&gt; 393

&lt;211&gt; 566

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 393

```

actagtcacg tgtggtggaa ttcgcggccg cgtcgacgga caggtcagct gtctggctca 60
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga ttaaattcag cctaaacggt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcccggca 180
gagaaggctc agtttgtcca tcagcattat catgatata ggactgggta cttgggttaag 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttggga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360
catttattaa tcatccttgc ctgtgtctat tattatattc atatctctac gctggaaact 420
ttctgcctca atgtttactg tgcccttgggt ttgtctagtt tgtgtgtgtg aaaaaaaaaa 480
cattctctgc ctgagtttta atttttgtcc aaagtattt taatctatac aattaaaagc 540
ttttgcctat caaaaaaaaa aaaaaa                                     566

```

&lt;210&gt; 394

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(384)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 394

```

gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaatng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttta ggagttttta gctgagtgtc actgtagacc ccaaatacca 180
tcccaagatt atcgggagaa agggggcagt aattacccaa atccggttgg agcatgacgt 240
gaacatccag tttctgata aggacgatgg gaaccagccc caggaccaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360

```

tgagcagatg gtttctgagg acgt

384

<210> 395

<211> 399

<212> DNA

<213> Homo sapiens

<400> 395

```

ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgac 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagaggt ttcattcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300
caagttctct ttggaaagcc tgggcatctc ctactacag acctctgacc atgggacggt 360
gcagcctggg gagaccatcc aatcccaaata aaaatgcac 399

```

<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

```

tggagttntc agtgcaaaca agccataaag cttcagtagc aaattactgt ctcacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcat'aactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaa gtggatgaat aatctggata ttttctctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gttttagggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt 403

```

<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(100)

<223> n = A,T,C or G

<400> 397

```

actagtnacg tgtgggtggaa ttcgcgggcg cgtcgacctc naanccatct ctatagcaaa 60
tccatccccg ctcttggttg gtnacagaat gactgacaaa 100

```

<210> 398

<211> 278

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(278)

<223> n = A,T,C or G

&lt;400&gt; 398

```

gcgggccgct cgacagcagt tccgccagcg ctgcgccctg ggtgggggatg tgctgcacgc 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgagggtg actcatcatg 180
ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

```

&lt;210&gt; 399

&lt;211&gt; 298

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(298)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 399

```

acggagggtg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60
gggggtgccng catggagcgc atggggcgcg gcctggggcca cggcatggat cgcgtgggct 120
ccgagatcga gcgcatgggc ctggctcatgg accgcatggg ctccgtggag cgcgtgggct 180
ccggcattga gcgcatgggc ccgctgggcc tcgaccacat ggcctccanc attgancgca 240
tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcattggg 298

```

&lt;210&gt; 400

&lt;211&gt; 548

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 400

```

acatcaacta cttcctcatt ttaaggatg gcagttccct tcctcccctt ttctgcctt 60
gtacatgtac atgtatgaaa ttctctctc ttaccgaact ctctccacac atcacaaggt 120
caaagaacca cagccttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180
tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240
tgcagagggc tagagaatta ttcatacag gctttgaggc caccatgtc acttatcccg 300
tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360
gttggeccca taattctggg cttttgttgt ttgttttaat tacttgggca tcccaggaag 420
ctttccagtg atctcctacc atgggcccc ctctgggat caagccccct ccaggccctg 480
tcccagccc ctctgcccc agcccaccgg ctgacctgg tgctcagccc tcccattggg 540
agcaggtt 548

```

&lt;210&gt; 401

&lt;211&gt; 355

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(355)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 401

```

actgtttcca tgttatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60
tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120
taagatgggt ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
tataaatgaa tggctgaag caaagtggcc atgggtggcg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnngg tttccaacca ggggaagggt 300

```

ccctttttgca ttgccaaagt ccataacccat gagcactact ctaccatggn tctgc 355

<210> 402

<211> 407

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(407)

<223> n = A,T,C or G

<400> 402

atgggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60  
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120  
aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180  
gaataaagat aaaaaagaga aggacattac aaaggtgggc ctgacctttg ataaatctca 240  
ttgcttgata ccaacctggg ctgttttaac tgcccaaacc aaaaggataa tttgctgagg 300  
ttgtggagct tctcccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360  
gntgattttg ctgacaactc cttttctgaa gttttactca ttccaa 407

<210> 403

<211> 303

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 403

cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatcc aggcacacaaa 60  
tcctaagcaa gagccatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120  
tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180  
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240  
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300  
gga 303

<210> 404

<211> 225

<212> DNA

<213> Homo sapiens

<400> 404

aagtgtaaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60  
attgttaatg cactcattta cctttacatg gtgaaagttc tctcttgatc ctacaaacag 120  
acattttcca ctctgttttc catagtgtgt aagtgtatca gatgtgttgg gcatgtgaat 180  
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcac 225

<210> 405

<211> 334

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(334)

<223> n = A,T,C or G

<400> 405

```
gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgaggggtg tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
tcatccccat cccatgccaa aggaagaccc tccctccttg gctcacagcc ttctctagge 180
ttcccagtgct ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcanng tggatcccac ccct 334
```

<210> 406

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(216)

<223> n = A,T,C or G

<400> 406

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tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcag gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant 216
```

<210> 407

<211> 413

<212> DNA

<213> Homo sapiens

<400> 407

```
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcacccagtgc tcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagtccc agaaaaagtt aaaacagaca atggggccagg ttctgtagta aag 413
```

<210> 408

<211> 183

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(183)

<223> n = A,T,C or G

<400> 408

```
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tncttaacta gttaatcctt aaagggtan ntaatcctta actagtcctt ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tatttactcc ttctggcta cccatgtact 180
ntt 183
```

<210> 409

<211> 250

<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(250)  
<223> n = A,T,C or G

<400> 409  
cccacgcatg ataagctctt tatctctgta agtcctgcta ggaaatcatc aaatctgacg 60  
gtgggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120  
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180  
gcttcccagt gcccccagga cagcgtgggc tatgtttaca gcgcntcctt gctggggggg 240  
ggcctatgc 250

<210> 410  
<211> 306  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(306)  
<223> n = A,T,C or G

<400> 410  
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60  
agtcttgcaa tccatttgc aggatccgtc tgtgcacatg cctctgtaga gagcagcatt 120  
cccagggacc ttggaaacag ttggcactgt aagggtgctt ctccccaaaga cacatcctaa 180  
aagggtgttg aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240  
nactggttg ctttttttgn atctttttta aactggaaag ttcaattgng aaaatgaata 300  
tcntgc 306

<210> 411  
<211> 261  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(261)  
<223> n = A,T,C or G

<400> 411  
agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60  
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120  
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180  
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240  
cttctctcaa ggngaggcaa a 261

<210> 412  
<211> 241  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(241)

<223> n = A,T,C or G

<400> 412

```
gttcaatggt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctgggagatt tctactgggtta cattgaattc ccaaactacc cangcaatta cccagccaac 240
a 241
```

<210> 413

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 413

```
aactcttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60
ctcatccaag ttcttagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t 231
```

<210> 414

<211> 234

<212> DNA

<213> Homo sapiens

<400> 414

```
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggt cttccttttg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaagctga ttcactatgg ggggagggtg attgaagtcc tcca 234
```

<210> 415

<211> 217

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(217)

<223> n = A,T,C or G

<400> 415

```
gcataggatt aagactgagt atcttttcta cattctttta acttttctaag gggcacttct 60
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cacttttcta 120
cacctagcaa tagtagaatt cagtctact tctgaggcca gaagaatggg tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc 217
```

<210> 416

<211> 213

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature  
 <222> (1)...(213)  
 <223> n = A,T,C or G

<400> 416  
 atgcataatnt aaagganact gcctcgcttt tagaagacat ctggnetgct ctctgcatga 60  
 ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120  
 cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180  
 atattggaac agatggagtc tctactacaa aag 213

<210> 417  
 <211> 303  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(303)  
 <223> n = A,T,C or G

<400> 417  
 nagtcttcag gcccatacagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60  
 gtgggaaagg ctttactctg agttcaaata ttcaagccca tcagagagtc cacactggag 120  
 agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180  
 ttcattctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240  
 tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300  
 agt 303

<210> 418  
 <211> 328  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(328)  
 <223> n = A,T,C or G

<400> 418  
 tttttggcgg tgggtggggca gggacgggac angagtctca ctctgttgcc caggctggag 60  
 tgcacaggca tgatctcgcc tcaactacaac ccctgcctcc catgtccaag cgattcttgt 120  
 gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180  
 gtatttttag tagagacagg gtttcacat gttggccagg ctggtctcaa actcctnacc 240  
 tcagnngtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300  
 aaagtgctan gattacaggc cgtgagcc 328

<210> 419  
 <211> 389  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(389)  
 <223> n = A,T,C or G

<400> 419  
 cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatatg 60



```

acccttgagc catggactgg agcctgaaag gcagcgtaca ccctgctcct gatcttgctg 120
cttgtttcct ctctgtggct ccattcatag cacagttggt gcaactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggc gtgccaggca 240
ccggttctcc agccaccaac ctcactcgct cccgcaaata gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360
tggcagccac tcnggctgtg tcgacgcgg 389

```

<210> 420

<211> 408

<212> DNA

<213> Homo sapiens

<400> 420

```

gttcctccta actcctgccg gaaacagctc tctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tctgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtgtg tgactttggt gtttcggcat ggagaccgaa 180
gtccattga cacttttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgtctatg acaaacctgg caagcccg 408

```

<210> 421

<211> 352

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(352)

<223> n = A,T,C or G

<400> 421

```

gtcaaaaaat ctttttactg atnngcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacagggtc ttttgggtc cttcttctcc accacnatac atttgcagtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacagggt tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcagtc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttcct gg 352

```

<210> 422

<211> 337

<212> DNA

<213> Homo sapiens

<400> 422

```

atgccaccat gctggcaatg cagcggggcg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcgatagcaa ggtgccggcg atcgcggcg cgtaaatcct ggccaaggtc agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggtc 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaattat 337

```

<210> 423

<211> 310

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature  
<222> (1)...(310)  
<223> n = A,T,C or G

<400> 423  
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60  
aggagaatga ggcctggcct gggagccctg tgcctactan aagcncatta gattatccat 120  
tcaactgacag aacagggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtc 180  
tccttcttga agattctttg gcagttgtct ttgtcataac ccacagggtg anaacaagg 240  
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300  
tccgagtta 310

<210> 424  
<211> 370  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(370)  
<223> n = A,T,C or G

<400> 424  
gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60  
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120  
cactgacaga acagggtctt tttgggtcct tcttctccac cacgatatac ttgcagtcct 180  
ccttcttgaa gattctttg cagttgtctt tgtcataacc cacagggtga gaaacatcct 240  
ggttgaatct cctggaactc ctcattagg tatgaaatag catgatgcat tgcataaagt 300  
cacgaagggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360  
tccgtcgacg 370

<210> 425  
<211> 216  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(216)  
<223> n = A,T,C or G

<400> 425  
aattgctatn ntttattttg ccaactcaaaa taattacca aaaaaaaaaa tnttaaatga 60  
taacaacnca acatcaaggn aananaaca ggaatggntg actntgcata aatnggccga 120  
anattatcca ttatnttaag gggtgacttc aggntacagc acacagacaa acatgcccag 180  
gaggntntca ggaccgctcg atgtntntg agggag 216

<210> 426  
<211> 596  
<212> DNA  
<213> Homo sapiens

<400> 426  
cttccagtga ggataaccct gttgccccgg gccgagggtc tccattaggc tctgattgat 60  
tggcagtcag tgatggaagg gtgttctgat cattccgact gcccgaaggg tcgctggcca 120  
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatgggtga 180  
gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240  
gacatcacgg caacttttaa tgaaatgatt tgaagggccca ttaagaggca cttcccgtta 300

ttaggcagtt catctgcact gataaacttct tggcagctga gctggtcgga gctgtggccc 360  
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420  
ggtggatggc cttttcagct ttaaccaat ttgcactgcc ttggaagtgt agccaggaga 480  
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540  
gtcccgtggt tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct 596

<210> 427

<211> 107

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(107)

<223> n = A,T,C or G

<400> 427

gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncaccag 60  
cccgggagca gccttanaga gtcctgttt gactgcccgg ctcagng 107

<210> 428

<211> 38

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(38)

<223> n = A,T,C or G

<400> 428

gaacttcena anaangactt tattcactat ttacatt 38

<210> 429

<211> 544

<212> DNA

<213> Homo sapiens

<400> 429

ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60  
attgaagagc ggctgcagcc ctgcggttca gattaaaaac cgagaattgt atagacgccg 120  
atatccacga actcttgaag gactttctga tttatccaca atcaaatcat cggttttcag 180  
tttggtggtt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcggt 240  
gccttccact tcagttacac ctcactcacc atcctctcct gttggttctg tgctgcttca 300  
agataactaag cccacatttg agatgcagca gccatctccc ccaattcttc ctgtccatcc 360  
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420  
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480  
acctcaacaa gttagagaga tatgcatatc cagggatttt ttgccagggt gtaggagaga 540  
ttat 544

<210> 430

<211> 507

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 430

```
cttatacncaa tggggctccc aaacttggt gtgcagtgga aactccgggg gaattttgaa 60
gaacactgac acccatcttc caccgcgaca ctctgattta attgggctgc agtgagaaca 120
gagcatcaat ttaaaaagct gccagaaatg ttntcctggg cagcgttggt atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgttttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtga tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctcctc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa 507
```

<210> 431

<211> 392

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 431

```
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtcctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggtcttttac tctgctgttt ct 392
```

<210> 432

<211> 387

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(387)

<223> n = A,T,C or G

<400> 432

```
ggtatccta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcgga gtccagccac tngaaacat gtcctcttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tattttgctt ctgtctgnga 240
attctgttgc ttctggggca tttccttgng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt 387
```

<210> 433

<211> 281

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(281)

<223> n = A,T,C or G

<400> 433

```
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagnagg ntctctgtnt gccactggg 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281
```

<210> 434

<211> 484

<212> DNA

<213> Homo sapiens

<400> 434

```
ttttaaaata agcatttagt gctcagtcct tactgagtac tctttctctc cctcctctctg 60
aatttaattc ttcaacttg caatttgcaa ggattacaca ttctactgtg atgtatattg 120
tgttgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatgggtc tcagaaccat ttcacccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag tacccatgtc 480
ttta 484
```

<210> 435

<211> 424

<212> DNA

<213> Homo sapiens

<400> 435

```
gcgccgctca gagcagggtca ctttctgcct tccacgtcct ccttcaagga agccccatgt 60
gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcaggtgtc ggggtgacct 240
cttgagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaaacctc ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac 424
```

<210> 436

<211> 667

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(667)

<223> n = A,T,C or G

<400> 436

```
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcttgcccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacaggggt 300
gccagggttg tcatagcact catcaaagtc cgggtcaacgt ctgtgcttcg aatataaacc 360
```

```

tgttcatgtt tataggactc attcaagaat tttctatata tcttttcttat atactctcca 420
agttcataat gctgctccat gcccagctgg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaaagggt tcaatgggac ttcgggtctcc atgccgaaac 540
accaaagtca caaacttcaa ctccttggct agtacacttc ggtctagcca gaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tgttgag 667

```

&lt;210&gt; 437

&lt;211&gt; 693

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 437

```

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggtaactct ctattttcac ccctcttgct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatggt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttgggggggac agccagcatc tttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaaact gctgttgctc ctgaggtggg gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcactgag ggctgtgggg taccttgtgg tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc 693

```

&lt;210&gt; 438

&lt;211&gt; 360

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 438

```

ctgcttatca caatgaatgt tctcctgggc agcgttggtga tctttgccac cttegtgact 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcc aagaatcttc aagaaggagg 180
actgcaagta tatctgggtg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

```

&lt;210&gt; 439

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(431)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 439

```

gttcctnnta actcctgcc aaaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttct tggctagacc 120
gaagtgtact agccaaggag ttgaagtgtg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcattggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatataaaaa attcttgaat gagtctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag t 431

```

<210> 440  
<211> 523  
<212> DNA  
<213> Homo sapiens

<400> 440  
agagataaag cttaggtcaa agttcataga gtcccatga actatatgac tggccacaca 60  
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120  
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaacc cacaatctag ggtgggaaca 180  
aggaaggaaa gatgtgaata ggctgatggg caaaaacca atttaccat cagtccagc 240  
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300  
actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360  
taaaaattaa aacctctttg tgctccttgg tcttggaaac tttatgttcc ttttaaagaa 420  
acaaaaatca aactttacag aaagatttga tgtatgtaac acatatagca gctcttgaag 480  
tatatatatc atagcaaata agtcactctga tgagaacaag cta 523

<210> 441  
<211> 430  
<212> DNA  
<213> Homo sapiens

<400> 441  
gttcctccta actcctgcc aaacagctc tctcaacat gagagctgca cccctcctcc 60  
tggccagggc agcaagcctt agccttggtt tcttggttct gcttttttcc tggctagacc 120  
gaagtgtact agccaaggag ttgaagtgtg tgactttggt gtttcggcat ggagaccgaa 180  
gtccattga cacttttccc actgaccca taaaggaatc ctcatggcca caaggatttg 240  
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300  
gatatagaaa attcttgaat gactcctata aacatgaaca ggtttatatt cgaagcacag 360  
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420  
aatttagtag 430

<210> 442  
<211> 362  
<212> DNA  
<213> Homo sapiens

<400> 442  
ctaaggaatt agtagtgttc ccatcacttg tttggagtgt gctattctaa aagattttga 60  
tttcttgtaa tgacaattat attttaactt tgggtgggga aagagttata ggaccacagt 120  
cttcaacttct gatacttgta aattaactt ttattgcact tgttttgacc attagctat 180  
atgttttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240  
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300  
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360  
tc 362

<210> 443  
<211> 624  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(624)  
<223> n = A,T,C or G

<400> 443  
tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60

```

ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaacttgg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360
taacgcctac aaaacactta aacatagata acatagggtg aagtactatg tatctggtaac 420
atggtaaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgctaata 480
agtacagaga gagggcactt aaaccaacta agggcctgga gggaagggtt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatac                                     624

```

<210> 444

<211> 425

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(425)

<223> n = A,T,C or G

<400> 444

```

gcacatcatt nntcttgcac tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagagggttg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcacacctg gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggctcgacg cggccgcgaa tttagtagta 420
gtaga                                     425

```

<210> 445

<211> 414

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 445

```

catgtttatg nttttggatt actttgggca cctagtgttt ctaaatcgtc tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcattgtggc agattattgg atgtagtctt ctttaactag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggcttctcc tcttgtattt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaaa tcgacgcggc cgcgaattta gtag      414

```

<210> 446

<211> 631

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(631)



<223> n = A,T,C or G

<400> 446

```
acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcagggtgtg 120
atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtgggtggc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaaactttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccctg catttggtgt 540
aatctacacc aatgaaaaca tgtactacag ctatatattga ttatgtatgg atatatttga 600
aatagtatac attgtcttga tgttttttct g 631
```

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

```
ccttgggaaa antntcacaa tataaagggt cgtagacttt actccaaatt ccaaaaagggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcattgtt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccattgag 480
attcctttat ggggtcagtg ggaaagggtg caatgggact tcggtctcca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggcta gtacacttcg gtcta 585
```

<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

```
tgctcgtggg tcattctgan nnccgaactg accntgccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag 93
```

<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(706)

<223> n = A,T,C or G

<400> 449

```
ccaagttcat gctntgtgct ggacgctgga caggggggcaa aagcnnttgc tcgtgggtca 60
ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tcctagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggtcgggcg cgccccattc gccattcagg ctgcgcaact 240
gttggaagg gcgatcggtg cgggcctctt cgctattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaagt tgggtaacgc caggggtttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcattgcacg 420
cgtacgtaag cttggatcct ctagagcggc cgcctactac tactaaattc gcggccgcgt 480
cgacgtggga tccnactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctggggagg tggaggttgc aatgagctga gatcaggccn ctgcnccecca 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaa 706
```

<210> 450

<211> 493

<212> DNA

<213> Homo sapiens

<400> 450

```
gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttta aaggtaaaaa aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggtac ttacagacat gtcgccaata tcaactgcag 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ygtacaattc 240
caagtcaggt agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggg cgacgcggcc 480
gcgaatttag tag 493
```

<210> 451

<211> 501

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 451

```
ggcgcgctcc cattcgccat tcaggctgcy caactgttgg gaagggcgat cggcgcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattecgggc cgcgtcgacg tgggatacnc actgagagag 300
tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360
cgcncagac actcacagct actcaggagg ctgagaacag gttgaacctg ggagggtggag 420
gttgcaatga gctgagatca ggccnctgcn ccccagcatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501
```

<210> 452

<211> 51

<212> DNA

<213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(51)  
 <223> n = A,T,C or G

<400> 452  
 agacgggttc accnttacaa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453  
 <211> 317  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(317)  
 <223> n = A,T,C or G

<400> 453  
 tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60  
 acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatgggtc tcagaaccat 120  
 ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180  
 taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240  
 cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300  
 taccatgtc tttatta 317

<210> 454  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 454  
 ttcgaggtag aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60  
 taagccacgc cagctcttg aaggagtctt gaattctcct ctgtcactc agtagaacca 120  
 agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180  
 ccttcctttt tcagtgttcc aaagctctc acaatttcat gaacaacagc t 231

<210> 455  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 455  
 taccaaagag ggcataataa tcagtctcac agtaggggtc accatcctcc aagtgaaaaa 60  
 cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120  
 gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180  
 caaagaattt ctcatagcac agtcacaat acagggtctc tttctcctct a 231

<210> 456  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 456  
 ttggcaggta cccttacaaa gaagacacca taccttatgc gttattaggt ggaataatca 60  
 ttccattcag tattatcggtt attattcttg gagaaaccct gtctgtttac tgtaaccttt 120  
 tgcactcaaa ttcctttatc aggaataact acatagccac tatttacaaa gccattggaa 180

ccttttttatt tgggtgcagct gctagtcagct ccttgactga cattgccaag t 231

<210> 457

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 457

cgagggtaccc aggggtctga aaatctctnn tttantagtc gatagcaaaa ttgttcatca 60  
gcattcctta atatgatctt gctataatta gatttttctc cattagagtt catacagttt 120  
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180  
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggcttttgt g 231

<210> 458

<211> 231

<212> DNA

<213> Homo sapiens

<400> 458

aggtctggtt cccccactt ccactccct ctactctctc taggactggg ctgggccaag 60  
agaagagggg tggttaggga agccgttgag acctgaagcc ccaccctcta ccttccttca 120  
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttcaa 180  
ggtcctgggt taggcatttt ggggggccag accccaggag aagaagattc t 231

<210> 459

<211> 231

<212> DNA

<213> Homo sapiens

<400> 459

ggtaccgagg ctgcgtgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60  
ccttcgcgaa acctgtggtg gcccaccagt cctaaccgga caggacagag agacagagca 120  
gcectgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180  
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231

<210> 460

<211> 231

<212> DNA

<213> Homo sapiens

<400> 460

gcaggataaa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60  
cctatcaccc tattcttggg ggctgcttct tcacagtgat catgaagcct agcagcaaat 120  
cccacctccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180  
gtggagcttg gtcacgcctc cagtcacccc ctaccaggct taaggataga a 231

<210> 461

<211> 231

<212> DNA

<213> Homo sapiens

<400> 461

cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggaggggc 60

gcgtgtgctc cagaagagtg tgtgcatgcc agaggggaaa caggcgccctg tgtgtcctgg 120  
gtgggggttca gtgaggagtg ggaaattggt tcagcagaac caagccgttg ggtgaataag 180  
agggggattc catggcactg atagagccct atagtttcag agctgggaat t 231

<210> 462

<211> 231

<212> DNA

<213> Homo sapiens

<400> 462

aggtagccctc attgtagcca tgggaaaatt gatgttcagt ggggatcagt gaattaaatg 60  
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcac gcccaatctc atatgatgtg 120  
gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180  
tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a 231

<210> 463

<211> 231

<212> DNA

<213> Homo sapiens

<400> 463

tactccagcc tggtagacaga gcgagaccct atcacccccc cccacccccc caaaaaaaaa 60  
actgagtaga cagggtgtcct cttggcatgg taagtcttaa gtcccctccc agatctgtga 120  
catttgacag gtgtcttttc ctctggacct cgggtgtccc atctgagtga gaaaaggcag 180  
tggggagggtg gatcttccag tcgaagcggc atagaagccc gtgtgaaaag c 231

<210> 464

<211> 231

<212> DNA

<213> Homo sapiens

<400> 464

gtactctaag attttatcta agttgccttt tctgggtggg aaagttaac cttagtgtact 60  
aaggacatca catatgaaga atgtttaagt tggaggtggc aacgtgaatt gcaaacaggg 120  
cctgtctcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180  
gggtgccagc caccagctag atgctctgta acttctagge cccattttcc c 231

<210> 465

<211> 231

<212> DNA

<213> Homo sapiens

<400> 465

catgttggtg tagctgtggt aatgctggct gcattctcaga cagggttaac ttcagtcctc 60  
gtggcaaat agcaacaaat tctgacatca tatttatggt ttctgtatct ttgttgatga 120  
aggatggcac aatttttgct tgtgttcata atatactcag attagtccag ctccatcaga 180  
taaactggag acatgcagga cattagggta gtgtgttagc tctggtaatg a 231

<210> 466

<211> 231

<212> DNA

<213> Homo sapiens

<400> 466

caggtagcctc tttccattgg atactgtgct agcaagcatg ctctccgggg tttttttaat 60  
ggccttcgaa cagaacttgc cacataccca ggtataatag tttctaactat ttgcccagga 120  
cctgtgcaat caaatattgt ggagaattcc ctagctggag aagtcacaaa gactatagga 180  
aataatggag accagtccca caagatgaca accagtcggt gtgtgaggct g 231

<210> 467  
 <211> 311  
 <212> DNA  
 <213> Homo sapiens

<400> 467  
 gtacaccctg gcacagtcca atctgaactg gttcggcact catctttcat gagatggatg 60  
 tgggtggcttt tctccttttt catcaagact cctcagcagg gagcccagac cagcctgcac 120  
 tgtgccttaa cagaaggctc tgagattcta agtgggaatc atttcagtga ctgtcatgtg 180  
 gcatgggtct ctgcccgaagc tcgtaatgag actatagcaa ggcggctgtg ggacgtcagt 240  
 tgtgacctgc tgggcctccc aatagactaa caggcagtgc cagttggacc caagagaaga 300  
 ctgcagcaga c 311

<210> 468  
 <211> 3112  
 <212> DNA  
 <213> Homo sapiens

<400> 468  
 catttgtgtg ggagaaaaac agaggggaga tttgtgtggc tgcagccgag ggagaccagg 60  
 aagatctgca tgggtgggaag gacctgatga tacagagttt gataggagac aattaaaggc 120  
 tgggaaggcac tggatgcctg atgatgaagt ggactttcaa actggggcac tactgaaacg 180  
 atgggatggc cagagacaca ggagatgagt tggagcaagc tcaataacaa agtgggttcaa 240  
 cgaggacttg gaattgcatg gagctggagc tgaagttag cccaattgtt tactagttaga 300  
 gtgaatgtgg atgattggat gatcatttct catctctgag cctcaggttc cccatccata 360  
 aaatgggata cacagtatga tctataaagt gggatagatg atgatctact tcaactggtt 420  
 atttgaagga tgaattgaga taattttattt cagggtgccta gaacaatgcc cagattagta 480  
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&lt;211&gt; 2229

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 469

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 470

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&lt;211&gt; 812

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 471

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<213> Homo sapiens

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&lt;210&gt; 474

&lt;211&gt; 1594

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 474

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&lt;210&gt; 475

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<212> DNA  
<213> Homo sapiens

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<221> unsure  
<222> (33)  
<223> n=A,T,C or G

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<212> DNA  
<213> Homo sapiens

<400> 476

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aaaaaaaaaa aaaa 3434

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Met Asp Gly His Thr Asp Ile Trp Arg Asn His Met Asp Thr Pro Pro  
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Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr  
35 40 45

His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr  
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Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr  
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Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln  
130 135 140

<213> Homo sapiens

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln  
5 10 15

Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr  
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Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr  
65 70 75 80

Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser  
85 90 95

His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp  
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 Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser  
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<210> 479  
 <211> 222  
 <212> PRT  
 <213> Homo sapiens

<400> 479  
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 Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr  
 35 40 45  
 His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr  
 50 55 60  
 Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr  
 65 70 75 80  
 Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser  
 85 90 95  
 His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val  
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 Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val  
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 Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His  
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 Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala  
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 Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp  
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 Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala  
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 Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val  
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<210> 480  
 <211> 144  
 <212> PRT  
 <213> Homo sapiens

<400> 480  
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 Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg  
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 Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln  
                           65                          70                          75                          80  
 Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys  
                           85                          90                          95  
 Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly  
                           100                          105                          110  
 Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu  
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 Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly  
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<210> 481  
 <211> 167  
 <212> PRT  
 <213> Homo sapiens

<400> 481  
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 Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg  
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 Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser  
                           35                          40                          45  
 Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys  
                           50                          55                          60  
 Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro



65                      70                      75                      80  
 Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser Ser Trp Arg  
                                  85                      90                      95  
 Ala Leu Ala Glu Val Thr Gly Cys Ser Leu Gly Pro Leu Gly Leu Ala  
                                  100                      105                      110  
 Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys Trp Ser His  
                                  115                      120                      125  
 Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr Ala Ala Phe  
                                  130                      135                      140  
 Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu Trp Ala Ser  
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 Trp Leu Ser Arg Gly Arg Pro  
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&lt;210&gt; 482

&lt;211&gt; 143

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 482

Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val  
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 Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu  
                                  20                      25                      30  
 Arg Ala Ser Trp Leu Pro Gly Gly Gly Pro Gln Ala Ile Leu Gly Arg  
                                  35                      40                      45  
 Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly  
                                  50                      55                      60  
 Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe  
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 Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr  
                                  85                      90                      95  
 Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly  
                                  100                      105                      110  
 Ala Ser Gly Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys  
                                  115                      120                      125  
 Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly  
                                  130                      135                      140

&lt;210&gt; 483

&lt;211&gt; 143

&lt;212&gt; PRT

<213> Homo sapiens

<400> 483

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Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
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Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala
      20              25              30

Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
      35              40              45

Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
      50              55              60

Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
      65              70              75              80

Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
      85              90              95

Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
      100             105             110

Arg Leu Val Gln Ala Glu His Pro Pro Pro His Pro Leu Glu Glu Val
      115             120             125

Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys
      130             135             140

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<210> 484

<211> 30

<212> PRT

<213> Homo Sapien

<400> 484

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Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
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Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile
      20              25              30

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<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 485

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31

<210> 486

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 486

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27

<210> 487

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 487

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36

<210> 488

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 488

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33

<210> 489

<211> 19

<212> PRT

<213> Artificial Sequence

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<223> Made in a lab

<400> 489

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1

5

10

15

Ser Val Ala

<210> 490

<211> 20

<212> PRT

<213> Artificial Sequence

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<223> Made in a lab

<400> 490

Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys

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5

10

15

Leu Ser His Ser

20

<210> 491

<211> 20

<212> PRT

<213> Artificial Sequence

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<223> Made in a lab

<400> 491

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Thr	Gly	Phe	Thr												
			20												

<210> 492

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
1				5					10					15	
Leu	Ala	Ser	Leu												
			20												

<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
1				5					10					15	
Lys	Tyr	Arg	Gly												
			20												

<210> 494

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
1				5					10					15	
Leu	Met	Ile	Ser												
			20												

<210> 495

<211> 20

<212> PRT

<213> Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 495

Asp Ser Leu Met Thr Ser Phe Leu Pro Gly Pro Lys Pro Gly Ala Pro  
1 5 10 15  
Phe Pro Asn Gly  
20

&lt;210&gt; 496

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 496

Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu  
1 5 10 15  
Pro Pro Pro Pro Ala  
20

&lt;210&gt; 497

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 497

Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val  
1 5 10 15  
Ser Val Arg Val  
20

&lt;210&gt; 498

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 498

Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val  
1 5 10 15  
Val Pro Gly Arg  
20

&lt;210&gt; 499

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

<223> Made in a lab

<400> 499

Arg	Val	Val	Pro	Gly	Arg	Gly	Ile	Cys	Leu	Asp	Leu	Ala	Ile	Leu	Asp
1				5				10						15	
Ser	Ala	Phe	Leu												
			20												

<210> 500

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 500

Leu	Asp	Ser	Ala	Phe	Leu	Leu	Ser	Gln	Val	Ala	Pro	Ser	Leu	Phe	Met
1				5				10						15	
Gly	Ser	Ile	Val												
			20												

<210> 501

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 501

Phe	Met	Gly	Ser	Ile	Val	Gln	Leu	Ser	Gln	Ser	Val	Thr	Ala	Tyr	Met
1				5				10						15	
Val	Ser	Ala	Ala												
			20												

<210> 502

<211> 414

<212> DNA

<213> Homo Sapien

<220>

<221> misc\_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 502

caccatggag	acaggcctgc	gctggctttt	cctggctcgt	gtgctcaaag	gtgtccaatg	60
tcagtgggtg	gaggagtccg	ggggtcgcct	ggtcacgcct	gggacacctt	tgacantcac	120
ctgtagagtt	tttggaatng	acctcagtag	caatgcaatg	agctgggtcc	gccaggctcc	180
aggggaagggg	ctggaatgga	tcggagccat	tgataattgt	ccacantacg	cgacctgggc	240
gaaaggccga	ttnatnattt	ccaaaacctn	gaccacgggtg	gatttgaaaa	tgaccagtcc	300
gacaaccgag	gacacggcca	cctatttttg	tggcagaatg	aatactggta	atagtggttg	360
gaagaatatt	tggggcccag	gcacctgggt	caccgtntcc	tcagggcaac	ctaa	414

<210> 503

<211> 379

<212> DNA

<213> Homo Sapiens

<220>

<221> misc\_feature

<222> (1)...(379)

<223> n = A,T,C or G

<400> 503

atnccgatggt gcttgggtcaa aggtgtccag tgtcagtcgg tggaggagtc cgggggtcgc	60
ctggtcacgc ctgggacacc cctgacactc acctgcaccg tntctggatt ngacatcagt	120
agctatggag tgagctgggt ccgccaggct ccagggaagg ggctgggnata catcggatca	180
ttagtagtag tggtagatatt tacgcgagct gggcgaaagg ccgattcacc atttccaaaa	240
cctngaccac ggtggatttg aaaatcacca gtttgacaac cgaggacacg gccacctatt	300
tntgtgccag aggggggttt aattataaag acatttgggg cccaggcacc ctggtcaccg	360
tntccttagg gcaacctaa	379

<210> 504

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 504

Gly	Phe	Thr	Asn	Tyr	Thr	Asp	Phe	Glu	Asp	Ser	Pro	Tyr	Phe	Lys	Glu
1				5				10						15	
Asn	Ser	Ala													

<210> 505

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 505

Lys	Glu	Asn	Ser	Ala	Phe	Pro	Pro	Phe	Cys	Cys	Asn	Asp	Asn	Val	Thr
1				5				10						15	
Asn	Thr	Ala	Asn												
				20											

<210> 506

<211> 407

<212> DNA

<213> Homo Sapien

<400> 506

atggagacag gcctgcgctg gcttctcctg gtcgctgcgc tcaaagggtg ccagtgtcag	60
tcgctggagg agtcgggggg tcgcctggtc acgcctggga caccctgcac actcacctgc	120
accgtctctg gattctccct cagtagcaat gcaatgatct gggtcgccca ggctccaggg	180
aaggggctgg aatacatcgg atacattagt tatggtggtg gcgcatacta cgcgagctgg	240
gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt	300
ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtgattt tagtggtatg	360
ttgtggggcc caggcaccct ggtcaccgtc tcctcagggc aacctaa	407

<210> 507  
 <211> 422  
 <212> DNA  
 <213> Homo Sapien

<400> 507  
 atggagacag gcctgcgctg gcttctcctg gtcgctgtgc tcaaagggtg ccagtgtcag 60  
 tcgggtggagg agtccggggg tcgcctgggc acgcctggga caccctgac actcacctgt 120  
 acagtctctg gattctccct cagcaactac gacctgaact gggtcgccca ggctccaggg 180  
 aaggggctgg aatggatcgg gatcattaat tatgttggtg ggacggacta cgcgaaactgg 240  
 gcaaaaaggcc gggttcacat ctccaaaacc tcgaccaccg tggatctcaa gatcgccagt 300  
 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360  
 ggtccgtgct tgcgcattct gggcccaggc accctggtca ccgtctcctt agggcaacct 420  
 aa 422

<210> 508  
 <211> 411  
 <212> DNA  
 <213> Homo Sapiens

<220>  
 <221> misc\_feature  
 <222> (1) ... (411)  
 <223> n = A,T,C or G

<400> 508  
 atggagacag gcctgcgctg cttctcctgg tcgctgtgct caaagggtgc cagtgtcagt 60  
 cgggtggagg gtccgggggt cgcttggtca cgctgggac accctgaca ctcacctgca 120  
 cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccgccag gctccaggga 180  
 aggggctgga atggatcgga atcattggta ctcttggtga cacatactac gcgaggtggg 240  
 cgaaaggccg attcaccatc tccaaaacct cgaccacggt gcatntgaaa atcnccagtc 300  
 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360  
 ctggttatta taaaatctgg ggcccaggca ccctgggtcac cgtctccttg g 411

<210> 509  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 509  
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 1 5 10 15

<210> 510  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 510  
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile  
 1 5 10 15



<210> 511  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys  
 1 5 10 15

<210> 512  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 512

Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu  
 1 5 10 15

<210> 513  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 513

Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu  
 1 5 10 15

<210> 514  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 514

Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 1 5 10 15

<210> 515  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

&lt;400&gt; 515

Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg  
1 5 10 15

&lt;210&gt; 516

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 516

Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln  
1 5 10 15

&lt;210&gt; 517

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 517

Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met  
1 5 10 15

&lt;210&gt; 518

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 518

Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly  
1 5 10 15

&lt;210&gt; 519

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 519

Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys  
1 5 10 15  
Gly

&lt;210&gt; 520

&lt;211&gt; 25

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 520

Val	Gly	Glu	Gly	Leu	Tyr	Gln	Gly	Val	Pro	Arg	Ala	Glu	Pro	Gly	Thr
1				5				10						15	
Glu	Ala	Arg	Arg	His	Tyr	Asp	Glu	Gly							
			20				25								

&lt;210&gt; 521

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 521

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10						15	
Pro	Pro	Pro	Pro	Ala											
				20											

&lt;210&gt; 522

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 522

Leu	Leu	Val	Val	Pro	Ala	Ile	Lys	Lys	Asp	Tyr	Gly	Ser	Gln	Glu	Asp
1				5					10					15	
Phe	Thr	Gln	Val												
			20												

&lt;210&gt; 523

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1) ... (254)

&lt;223&gt; Xaa = any amino acid

&lt;400&gt; 523

Met	Ala	Thr	Ala	Gly	Asn	Pro	Trp	Gly	Trp	Phe	Leu	Gly	Tyr	Leu	Ile
1				5				10						15	
Leu	Gly	Val	Ala	Gly	Ser	Leu	Val	Ser	Gly	Ser	Cys	Ser	Gln	Ile	Ile
			20				25					30			
Asn	Gly	Glu	Asp	Cys	Ser	Pro	His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu
			35				40								45

Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln  
 50 55 60  
 Trp Val Leu Ser Ala Thr His Cys Phe Gln Asn Ser Tyr Thr Ile Gly  
 65 70 75 80  
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met  
 85 90 95  
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu  
 100 105 110  
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu  
 115 120 125  
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala  
 130 135 140  
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg  
 145 150 155 160  
 Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu  
 165 170 175  
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys  
 180 185 190  
 Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly  
 195 200 205  
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly  
 210 215 220  
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu  
 225 230 235 240  
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 245 250

&lt;210&gt; 524

&lt;211&gt; 765

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 524

atggccacag caggaaatcc ctggggctgg ttcttggggg acctcatcct tgggtgtcgca 260  
 ggatcgctcg tctctggtag ctgcagccaa atcataaacg gcgaggactg cagcccgcac 120  
 tcgcagccct ggcaggcggc actgggtcatg gaaaacgaat tgttctgctc gggcgctctg 180  
 gtgcacccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 240  
 ctgggectgc acagtcttga ggccgaccaa gagccaggga gccagatggg ggaggccagc 300  
 ctctccgtac ggcacccaga gtacaacaga cccttgctcg ctaacgacct catgctcatc 360  
 aagttggacg aatccgtgct cgagtctgac accatccgga gcatcagcat tgcttcgcag 420  
 tgccctaccg cggggaactc ttgcctcggt tctggctggg gtctgctggc gaacggcaga 480  
 atgcctaccg tgcctgcagt cgtgaacgtg tcggtggtgt ctgaggaggt ctgcagtaag 540  
 ctctatgacc cgctgtacca ccccagcatg ttctgcgcgc gcggaggggc agaccagaag 600  
 gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 660  
 gtgtctttcg gaaaagcccc gtgtggccaa gttggcgtgc caggtgtcta caccaacctc 720  
 tgcaaattca ctgagtggat agagaaaacc gtccaggcca gtttaa 765

&lt;210&gt; 525

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 525

Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile  
 1 5 10 15  
 Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile  
 20 25 30  
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu

35	40	45
Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln		
50	55	60
Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly		
65	70	75
Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met		
85	90	95
Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu		
100	105	110
Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu		
115	120	125
Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala		
130	135	140
Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg		
145	150	155
Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu		
165	170	175
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys		
180	185	190
Ala Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly		
195	200	205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly		
210	215	220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu		
225	230	235
Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser		
245	250	

&lt;210&gt; 526

&lt;211&gt; 963

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 526

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atgagttcct gcaacttcac acatgccacc tttgtgctta ttggtatccc aggattagag 60
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aactgcatcg tgggtcttcat cgtaaggacg gaacgcagcc tgcacgctcc gatgtacctc 180
tttctctgca tgcttgacgc cattgacctg gccttatcca catccaccat gcctaagatc 240
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gcccagattg gcatcggtggc tgtggtcgcg ggatccctct tttttttccc actgcctctg 480
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caggatgtaa tgaagttggc ctatgcagac actttgccc aatgtgtata tgggtcttact 600
gccattctgc tgggtcatggg cgtggacgta atgttcatct ccttgtccta ttttctgata 660
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gtgtcacaca ttggtgtggt actgccttc tatgtgccac ttattggcct ctcatgtgta 780
cacgcctttg gaaacagcct tcatccatt gtgcgtgttg tcatgggtga catctacctg 840
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cgggtgctgg ctatgttcaa gatcagctgt gacaaggact tgcaggctgt gggaggcaag 960
tga 963

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&lt;210&gt; 527

&lt;211&gt; 320

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 527

Met Ser Ser Cys Asn Phe Thr His Ala Thr Phe Val Leu Ile Gly Ile  
                   5                  10                  15  
 Pro Gly Leu Glu Lys Ala His Phe Trp Val Gly Phe Pro Leu Leu Ser  
                   20                  25                  30  
 Met Tyr Val Val Ala Met Phe Gly Asn Cys Ile Val Val Phe Ile Val  
                   35                  40                  45  
 Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met  
                   50                  55                  60  
 Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile  
                   65                  70                  75                  80  
 Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Phe Glu Ala Cys  
                   85                  90                  95  
 Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr  
                   100                  105                  110  
 Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro  
                   115                  120                  125  
 Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly  
                   130                  135                  140  
 Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu  
                   145                  150                  155                  160  
 Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser  
                   165                  170                  175  
 Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu  
                   180                  185                  190  
 Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val  
                   195                  200                  205  
 Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val  
                   210                  215                  220  
 Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys  
                   225                  230                  235                  240  
 Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly  
                   245                  250                  255  
 Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg  
                   260                  265                  270  
 Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro  
                   275                  280                  285  
 Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala  
                   290                  295                  300  
 Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys

305 310 315 320

<210> 528  
<211> 20  
<212> DNA  
<213> Homo Sapien

<400> 528  
actatgggtcc agaggctgtg 20

<210> 529  
<211> 20  
<212> DNA  
<213> Homo Sapien

<400> 529  
atcacctatg tgccgcctct 20

<210> 530  
<211> 1852  
<212> DNA  
<213> Homo sapiens

<400> 530  
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tttcctctga gaactgcaac aataaataca aggatgctgg attttgtcaa atgccttttc 180  
tgtgtctgtt gagatgctta tgtgactttg cttttaattc tgtttatgtg attatcacat 240  
ttattgactt gcctgtgtta gaccggaaga gctgggggtg ttctcaggag ccaccgtgtg 300  
ctgcggcagc ttccgggataa cttgaggctg catcactggg gaagaaacac aytctgtcc 360  
gtggcgctga tggctgagga cagagcttca gtgtggcttc tctgcgactg gcttcttcgg 420  
ggagtctctc cttcatagtt catccatag gctccagagg aaaattatat tattttgtta 480  
tggatgaaga gtattacgtt gtgcagatat actgcagtgt cttcatctct tgatgtgtga 540  
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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 531

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&lt;210&gt; 532

&lt;211&gt; 292

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 532

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Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
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Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp
      50              55              60

Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu
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Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg
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Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp
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Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
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Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
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Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu
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Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile
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Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu  
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Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu  
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Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu  
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Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys  
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Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp  
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 <213> Homo sapiens

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<400> 534  
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&lt;210&gt; 535

&lt;211&gt; 6082

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 535

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&lt;211&gt; 6140

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;223&gt; n=A,T,C or G

&lt;400&gt; 536

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<213> Homo sapiens

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Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr Asp Pro Met Asp Ser	115		120		125	
Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr Val Leu Thr Phe Cys	130		135		140	
Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr Phe Tyr His Val Gln	145		150		155	160
Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys His Met Ile Tyr Arg	165		170		175	
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Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn Lys Phe Asp Gln Val	195		200		205	
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Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile Thr Asn Leu Arg Lys	290		295		300	
Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys Leu Arg Gly Met Asn	305		310		315	320
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Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr Ala Ser Arg Val Phe	340		345		350	
Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu Thr Val Thr Leu Phe	355		360		365	
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 Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu  
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 Ala His Gln Asp Leu His Ser Glu Ala Trp Phe Leu Phe Leu Thr Thr  
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Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser Leu Ile Ser Ala Leu 1075 1080 1085		
Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp Ile Asp Lys Ile Leu 1090 1095 1100		
Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile 1105 1110 1115 1120		
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Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu 1140 1145 1150		
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Ile	Ala	Arg	Ser	Leu	Leu	Val	Phe	Tyr	Val	Leu	Val	Asn	Ser	Ser	Gln
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Val	Ile	Pro	Trp	Ile	Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe
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&lt;210&gt; 545

&lt;211&gt; 18

&lt;212&gt; PRT

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&lt;400&gt; 545

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Ser Val

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&lt;211&gt; 29

&lt;212&gt; PRT

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Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met  
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&lt;210&gt; 547

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&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 547

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Cys Arg Met Pro Arg Thr Leu Arg Arg Leu  
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&lt;210&gt; 548

&lt;211&gt; 18

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 548

Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu



200

5

10

15

Glu Cys

&lt;210&gt; 549

&lt;211&gt; 18

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 549

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Gln Ala

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&lt;211&gt; 14

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&lt;400&gt; 550

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&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 551

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(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
17 May 2001 (17.05.2001)

PCT

(10) International Publication Number  
**WO 01/34802 A3**

(51) International Patent Classification<sup>7</sup>: C12N 15/12,  
15/62, 15/11, 1/21, 5/10, C07K 14/47, 16/18, 19/00, A61K  
38/17, 31/70, 39/395, 48/00, G01N 33/68, C12Q 1/68

(21) International Application Number: PCT/US00/30904

(22) International Filing Date:  
9 November 2000 (09.11.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
09/439,313 12 November 1999 (12.11.1999) US  
09/443,686 18 November 1999 (18.11.1999) US

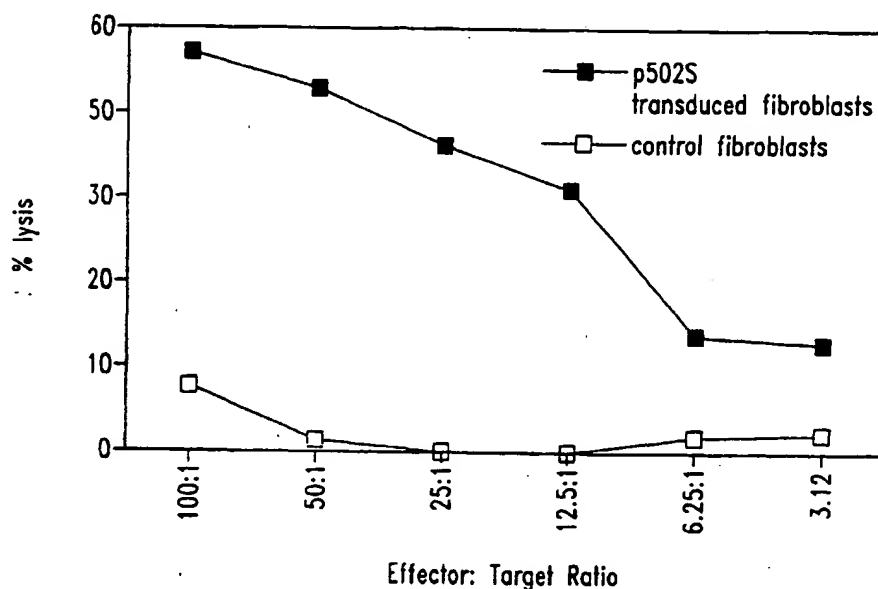
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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.



WO 01/34802 A3



(81) **Designated States (national):** AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— with international search report

(88) **Date of publication of the international search report:**  
4 April 2002

(84) **Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 00/30904

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C12N15/62 C12N15/11 C12N1/21 C12N5/10  
C07K14/47 C07K16/18 C07K19/00 A61K38/17 A61K31/70  
A61K39/395 A61K48/00 G01N33/68 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBL, BIOSIS, WPI Data, SEQUENCE SEARCH

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 37093 A (CORIXA CORP) 27 August 1998 (1998-08-27)	1-11, 14-24, 60,61, 63,64 25-41
Y	the whole document ---	
X	WO 98 37418 A (CORIXA CORP) 27 August 1998 (1998-08-27) the whole document ---	1-11, 42-64
X	DATABASE EMBL [Online] Accession no AF047020 Sequence ID AF047020, 20 February 1998 (1998-02-20) ALBERS C ET AL: "Human alpha-methylacyl-CoA racemase cDNA sequence" XP002176408 abstract ---	1-11,60, 61,63,64
-/-		

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

4 September 2001

Date of mailing of the international search report

15.01.02

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## INTERNATIONAL SEARCH REPORT

Inter. Application No

PCT/US 00/30904

## C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 317 141 A (BECTON DICKINSON CO) 24 May 1989 (1989-05-24) the whole document	34-36
Y	--- SCHMIDT-WOLF G D ET AL: "Activated T cells and cytokine-induced CD3+CD56+ killer cells." ANNALS OF HEMATOLOGY, vol. 74, no. 2, 1997, pages 51-56, XP002176407 ISSN: 0939-5555 the whole document	34-36
A	--- WO 97 33909 A (CORIXA CORP) 18 September 1997 (1997-09-18)	
Y	--- SJOGREN H O: "Therapeutic immunization against cancer antigens using genetically engineered cells" IMMUNOTECHNOLOGY, ELSEVIER SCIENCE PUBLISHERS BV, NL, vol. 3, no. 3, 1 October 1997 (1997-10-01), pages 161-172, XP004097000 ISSN: 1380-2933 the whole document	25-33, 37-41
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E	--- WO 01 25272 A (CORIXA CORP ; REED STEVEN G (US); XU JIANGCHUN (US); CHEEVER MARTIN) 12 April 2001 (2001-04-12) claims -----	1-11, 14-64

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/30904

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 23 24 31-33 36 37 39-41 are (partially) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Claims 1-11, 14-64, partially.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1: Claims 1-11 14-64 partially

A polypeptide comprising at least an immunogenic portion of a prostate tumor protein defined as SEQ ID 108 and which is encoded by the related SEQ IDs 2,3,107 (according to the Description of the Sequence Identifiers), fragments and variants thereof, fusion proteins comprising it, polynucleotides or oligonucleotides derived therefrom, antibodies or fragments thereof binding to the polypeptide, pharmaceutical compositions or vaccines comprising these products and their use in methods for inhibiting, monitoring or diagnosing the development of a prostate cancer, for removing tumor cells from a sample or for expanding and/or stimulating T-cells.

2. Claims: Inventions 2-450: Claims 1-64 (all partially and as far as applicable)

As for subject 1 but concerning respectively SEQ IDs 1,4-106,109-111,115-171,173-175,177,179-305,307-315,326,328,330,332-335,340-375,381,382,384-476,524,526,530,531,533,535 and 536.

## INTERNATIONAL SEARCH REPORT

...formation on patent family members

International Application No

PCT/US 00/30904

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